# CELLS FROM ICONS TO SYMBOLS
# MOLECULARISING CELL BIOLOGY IN THE 1980s

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"You did not have any. You did not even have a whole living image, which you could have, if only externally, copied. What was there left for you to do? To grab the first trait that happened to flash into your mind. Your mind is stored full of such things, ready for any occasion in life. Every impression, in some form or another, remains in our memories, and can be used when needed. In such harried and general descriptions we care very little whether what we transmit corresponds to reality. We are satisfied with any general characteristic or illusion. To bring images to life, daily practice has produced for us stencils or external descriptive signs, which, thanks to long usage, have become intelligible to everyone."

**Constantin Stanislavski**
**An Actor Prepares (1936)**

"Llega un momento en que cualquier realidad se acaba. Y entonces no hay mas remedio que inventarla."
("There is a point in which any reality does exhaust itself. And then there is no other option than to invent it")

**Mario Benedetti**
**El Porvenir de mi pasado (2003)**

In memoriam

Jorge Eduardo Bosch
Mariano Levin

*Ceci n'est pas une cellule*

**Declaration of originality.**

I, Norberto Serpente declare that the work presented in this dissertation is my own, and that any ideas, quotations or other material taken directly or indirectly from the work from other authors have been properly acknowledged and referenced.

Signed: Norberto Serpente

Date:

**THESIS ABSTRACT**

This thesis addresses the visual change that began to take place in cell biology by the early 1980's as manifested in textbooks. From that time onwards images produced by instruments of a different nature to the optical and electronic microscopes began to compete for visual supremacy. An important consequence of this visuality shift has been the creation of epistemic discontinuity inside the discipline. New areas, such as signal transduction, fully dependent on this kind of visuality began to emerge.

The thesis places and argues for this visual shift as occurring in the context of the following related co-productive developments during the 1960s to 1980s: The promotion and expansion of the project of molecularisation into cell biology. The occurrence of deep changes in academic institutions, oriented to mimic industrial set ups based on network functioning and more flexible forms of production. The emergence of textbooks to better prepare newcomers to the discipline for the production needs of the laboratory. An extensive use of new techniques mainly from molecular biology, biochemistry and immunology. And last but not least, the emergence of a new type of scientific self armoured with a new set of moral codes and attitudes.

The study is based on a visual examination of the images contained in the different editions (from 1983 to 2008) of the textbook *Molecular Biology of the Cell* (MBC) by Alberts et al, as the book that heralded molecularisation inside cell biology. The imagery displayed in this textbook is compared with the different editions (from 1948 to 1987) of the originally entitled *General Cytology* textbook of De Robertis et al, the book that belonged to the microscopical tradition of thought.

The theoretical framework I am using to understand this visual shift as occurring in textbooks is based on semiotics and simulation theory.

This dissertation argues that the visual change that the discipline of cell biology began to endure from the early 1980s entails an overall substitution of signs from iconic to symbolic forms and that the new symbolic imagery builds its authenticity and gains its widespread acceptance not only from its experimental validity, but also from the traces they contain derived from both indexical and iconic forms. In a more explorative tone I argue that this new symbolic cell biology is at risk of becoming a self-referential system with a remote relationship with the experimental arrangement it originates from.

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**Thesis content**

**List of Abbreviations**

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| **CB** | *Cell Biology* |
| **CMB** | *Cellular and Molecular Biology* |
| **CSH** | Cold Spring Harbour |
| **DNA** | Deoxyribonucleic acid |
| **GFP** | Green fluorescent protein |
| **GTP** | Guanosine triphosphate |
| **IBYME** | Instituto of Biologia y Medicina Experimental |
| **IP** | Immunoprecipitation |
| **IP/WB** | Immunoprecipitation, Western Blotting |
| **JLI** | Julian Lewis interview |
| **KRI** | Keith Roberts interview |
| **MBC** | *Molecular Biology of the Cell* |
| **MBG** | *Molecular Biology of the Gene* |
| **MRI** | Martin Raff interview |
| **RCA** | Radio Corporation of America |
| **RNA** | Ribonucleic acid |
| **SDS-PAGE** | Sodium dodecyl sulphate polyacrylamide electrophoresis |
| **TIBS** | Trends in Biochemical Sciences |
| **TEM** | Transmittion electron microscopy |
| **WB** | Western blotting |
| **YTHS** | Yeast Two Hybrid System |

**Outline of chapters.**

This dissertation examines a visual change that occurred in the discipline of cell biology between the 1950s and the 2000s as manifested in textbooks. It argues that a microscope based imagery, dominant since the emergence of cell theory in the 1830s began to lose that dominance in the early 1980s at the hands of molecular imagery.

A sound assessment of what exactly the visual change entails requires first of all a definition of the two main imageries involved in it. This is the main objective of Chapter 1, which after reviewing all the different types of images featuring in cell biology textbooks from the 1950s to the 2000s, provides for the two main imageries identified, the microscopical and the molecular  a brief historical overview of their respective emergence and development, the instruments from which they originate, together with their organising principles and metaphors. Beginning with the microscopic imagery the chapter traces the origins of the optical images of cells since 1660s through the times of the emergence of cell theory in the 1830s to the 1940s ending with the 1950s the period when the electron microscope emerged. The chapter then continues with a similar analysis for the molecular imagery for which a historical classification of all its forms is proposed. This classification is based on three historical zones of epistemic convergence between the interests of molecular culture in its different forms through history (organic/physiological chemistry, biochemistry, molecular biology) and those of cell biology. For each of these it proposes the existence of three types of visual forms of molecular imagery. These three historical zones of epistemic convergence (waves of molecularisation) and their respective imageries are contextualised respectively with the following three key events for the history of cell biology namely: a) the paradigmatic change from colloidal to corpuscular chemistry (1900s-1930s), b) the fusion of biochemical and cellular explanation (sub-cellular localisation of metabolic cycles), alongside the appearance of the first 3D models from molecular biology (1930s-1970s), and c) the fulfilment of the epistemic need of molecular biology to test the universal validity of the molecular mechanisms described in bacteria and viruses in higher organisms, by the use of the, at the time, new technique of genetic engineering and other biochemical techniques (1970s-2000s). The chapter closes with a discussion of the

process of translation of the visual outputs of the instruments used into the creation of the imagery involved in the visual change.

Since this dissertation argues that the main carrier for the visual change was textbooks, the main aim of Chapter 2 is to investigate how they looked at the epistemic and visual level before the visual change and how this condition changed through time. After a justification of why textbooks were selected as source of analysis for the visual change, the chapter begins by exploring visually and epistemically the development of both imageries in De Robertis et al *Cell Biology* (CB). A book that constitutes the best exemplar of the dominance of the microscopical tradition of the 20$^{th}$ century before the emergence of the latest face of molecularisation of cell biology as a consequence of 'the molecular revolution of the late 1970s. This is done by quantitatively analysing the number of images contained in a selection of chapters in this textbook throughout its successive editions (from 1948 to 1987).

Chapter 3,'The making of an icon', is devoted to unravelling the many aspects of the process of production of *Molecular Biology of the Cell* (MBC), the main vehicle for the standardisation of images of the molecular culture in cell biology. Based on interviews with three of the authors of the textbook, the chapter highlights all the novelty the book brought about during its production. The aim here is to show in detail the network-based practices that the authors set in motion for the writing of the chapters as well as the development of the program of image production at stake during its production. The chapter examines the emergence in the first edition of the textbook (1983) of the first forms of third-generation models of molecular imagery and its further expansion throughout its successive editions. The chapter ends with a discussion on the relationship between the networked imagery describing cell functioning featuring in MBC and the networked style manifested in the inner-workings of its production among the authors themselves and other participants, such as students and the extensive hub of 'hidden collaborators'.

The theoretical and historical framing to be used in this dissertation for the interpretation of the visual change is presented in Chapter 4, 'How to read the visual

change'. The central purpose of the chapter is to introduce alternative ways of reading the imagery of cell biology past and present. Since imagery cannot be separated from issues of 'representation' in science, the chapter begins with a short overview of the different kind of approaches to issues of 'representation' in science in general and biology in particular. The chapter introduces semiotic theory (Peirce, Barthes and Joly) to substantiate two important arguments raised in this study, namely: the conceptualisation of the visual change as one entailing a move from iconic towards symbolic forms and the capacity of molecular imagery to be meaningful with some independence of the models it contains. Grounded on recent work on the historical dimension of objectivity (Daston and Galison, 2007) it is also argued that the visual shift from microscopical to molecular imagery in cell biology corresponds to a shift where the image is taken as artifactual and as a tool directed to object manipulation rather than as a representation with some degree of a fidelity to nature. The chapter ends with a discussion on the applicability of the context of justification as defined in traditional philosophy of science to images, especially to molecular images.

The main task of Chapter 5, 'Cultures of knowing and cultures of image making in cell biology', is to highlight the importance of epistemic cultures and its actors, 'scientific selves', for the production of images in cell biology. The chapter begins with a brief description of the internal epistemic needs of molecular biology and the technological developments that allowed the proliferation of molecular imagery from the 1980s. The chapter continues with an account of some aspects of the scientific life of Eduardo Patricio De Robertis, main author of CB and a key 'scientific self' of the 20$^{th}$ century microscopical tradition, The chapter then proceeds to do the same for James Watson a central figure for the process of molecularisation of biology in general and cell biology in particular. Special attention is directed to his formative years at Harvard (1956-1978) when important changes began to be promoted in academia aimed to facilitate the expansion and development of the molecular sciences. The chapter describes key skills developed by Watson when he wrote his first textbook, *Molecular Biology of the Gene*, the forerunner of MBC. Grounded on recent work on the historical dimension of 'objectivity' (Daston and Galison, 2007) and 'scientific life' (Shapin 2008) this chapter makes a case for an intimate association between the visual change and a shift in

moral attitudes and normative codes of conduct enacted by scientists. Phrased differently, the two frame periods that of 1940s-1970s and that of 1980s-2000s are characterised by two distinctive types of 'scientific selves' represented by De Robertis and Watson respectively. The chapter shows how the 'scientific selves' of molecularisation, began to display more flexible ways of interaction, based on entrepreneurship, risk-taking, team-work and networking; all main attributes that characterise an emergent 'network based society' and the transformation of 'science as vocation' to 'science as a profession'.

Finally, Chapter 6 begins by presenting a series of wider socio-cultural developments such as flexible ways of production and the network society that may be related to emergence and development of the visual change. The chapter then introduces in a more speculative tone, Baudrillard's writings on hyperreality, in order to reflect on the possible self-referential condition created by the proliferation of molecular imagery in cell biology. The aim is to evaluate the state of the relationship between molecular visuality and the experimental world from which it arose alongside the neglect of other forms of imagery, such as that of the cellular model.

# INTRODUCTION

## THE RESEARCH PROBLEM

This dissertation addresses a change in the imagery displayed by the discipline of cell biology beginning in the 1980s **(Figure 1)**. Examples are derived from an examination of the images present in cell biology textbooks written in the English language and published mainly in Britain, and the USA from the 1950s to the 2000s. The examination of current editions reveals the occurrence of two main distinctive types of images. Images of cells attained with microscopes, either optical or electronic, and images of molecular models of cells attained with instruments and techniques that produce a visual output of a different nature to that of microscopes. Equally noticeable in current editions is that images of a molecular nature outnumber those produced by microscopes. An extension of this visual examination to different editions of cell biology textbooks from the 1950s onwards allows us to appreciate that this present pattern only began to emerge in the late 1970s and early 1980s and that this molecular imagery has kept growing ever since.[1] This study constitutes a departure from traditional studies on cell biology in two senses. On the one hand, it focuses more on visual discontinuities rather than epistemic ones, and on the other, it applies non-conventional interpretative frameworks, such as semiotics and cultural and simulation theory to respectively conceptualise the images at play and to understand the observed visual discontinuity in cell biology.[2]

## PURPOSE AND SIGNIFICANCE OF THIS DISSERTATION

This dissertation speaks of and sets out to explore the visual history of cells. Cells have been throughout history viewed, depicted, represented and presented in different ways. These visions, depictions representations and presentations have hinged on the

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1 In particular that of signal transduction and cell membrane embedded receptors with signalling function. Signal transduction refers to the intracellular events that occur inside a cell after an external substance interacts with a specific membrane embedded receptor, a condition that changes gene expression in the nucleus of the cell and consequently its behaviour. (See Chapter 1).

2 Two main directions characterise previous studies on the history of cytology (how the discipline was known before the 1960s). Those on the emergence and establishment of cell theory, see Arthur Hughes, *A history of cytology*. London, New York, Abelard and Schuman, 1959. Henry Harris, *The birth of the cell*, New Haven, Yale University Press, 1999). And those dealing with the merge of biochemistry and cytology during the period between the 1940s and the 1960s, see William Bechtel, *Discovering cell mechanisms: The creation of modern cell biology*, Cambridge, Cambridge University Press, 2006.

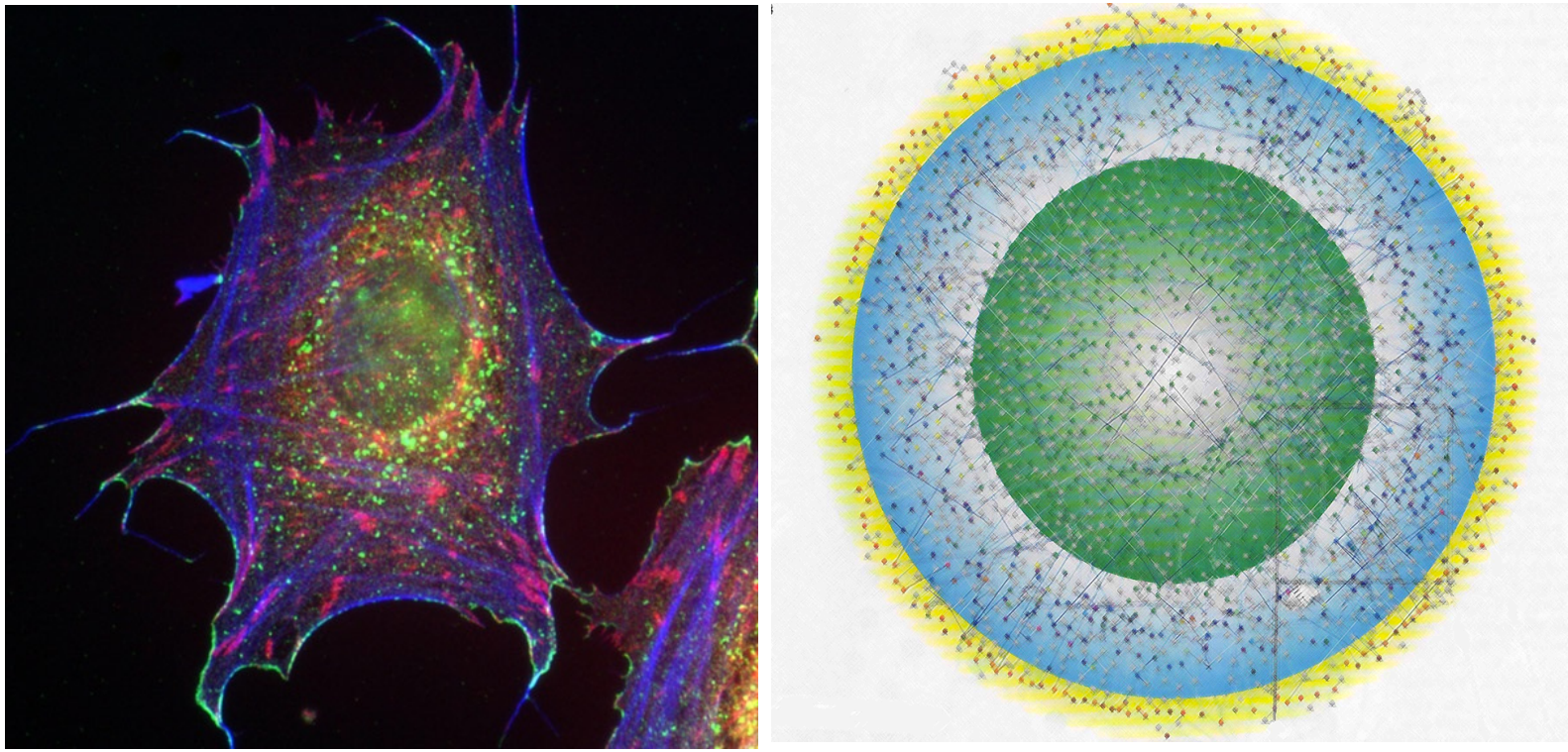

**Figure 1: The Visual Change in Cell Biology: From the microscopic to the molecular image**

following factors: a) different techne,[3] b) changes in the internal epistemic needs of the discipline of cell biology,[4] c) the interests of the different epistemic cultures that conform the discipline, and finally wider factors of a social nature (socio-ecomomic conditions of production).

By exploring the articulation of all these factors, especially the microscopical and molecular cultures of knowledge production this dissertation aims to show the mutual influence between all the factors mentioned above to create the present condition on the visual landscape of cell biology where the molecular image reigns supreme over the microscopical image.

Although the process of stabilisation and acceptability of images originated by microscopes (standardisation) has been extensively covered, the same process for molecular imagery has received scant, if no attention.[5] A key aim of this dissertation is to correct for that deficit by highlighting some key aspects of this process of standardisation of the latest visual form stemming from molecular culture; how it emerged, how it was constructed and how it became accepted and established.

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3 I use the term 'techne' to refer to the combination of instrument and technique (such as microscope plus fixation and staining).

4 Cell Biology possess the typical characteristics of traditional scientific disciplines, that is, it: a) a focus into a particular subject, b) uses of a distinctive set of methodologies, c) is practiced by a group of scientists that share that conformation of knowledge, d) is practiced at particular institutions and e) has an arrangement of journals and professional societies. Cell biology was known as cytology before circa the early 1960s. (Bechtel, 2006, op. cit., pp. 258-77). By internal cultures I refer to two, the microscopical and the molecular. Their characteristics and differences will be defined later in this introduction and with more depth in Chapter 1 and in Chapter 5 by focusing on the scientific selves that enact those cultures.

5 Important works have been produced on the acceptability and trustability of the microscopical imagery. See for example on the optical microscope, Stephen Jacyna, 'John Goodsir and the making of cellular reality'. *Journal of the History of Biology*, 1983, 16: 75-99. Jutta Schickore, *The microscope and the eye: A history of reflections*, 1740-1870, Chicago, London, The University of Chicago Press, 2007. And on the electron microscope Nicolas Rasmussen, 'Facts, artifacts, and mesosomes: Practising epistemology with the electron microscope. *Studies in History and Philosophy of Science*, 1993, 24: 227-65. Nicolas Rasmussen, 'Mitochondrial structure and the practice of cell biology in the 1950s. *Journal of the History of Biology*, 1995, 28, (281-429). Nicolas Rasmussen, *Picture control: The electron microscope and the transformation of biology in America, 1940-1960*, Stanford, California Stanford University Press, 1997. It is the standardisation of the latest forms of molecular imagery that is in need of assessment.

Although much is known about the previous visual forms displayed by molecular culture through history such as 2D paper formula and 3D models of DNA and proteins, nothing is known about its more recent expressions.[6] This dissertation aims to remedy that deficit by proposing that the molecular imagery that began to emerge in cell biology from the late 1970s constitutes the latest visual expression of molecular culture.[7]

To put it briefly, this dissertation aims to show how much in a period of thirty years (1970-2000) cell biology has changed visually through the input of molecular culture.[8] Its central aim is to understand the nature of this imagery change by posing the following questions: In what aspects do the microscopical and molecular imagery differ from each other? What were the internal epistemic needs for this imagery change? What are the differences between the 'scientific selves'[9] that were involved in its production? What were the basic underlying principles, cultural and epistemic that supported it? What could be the putative consequences for the biosciences of this change? In trying to answer these questions it is assumed that all these different phenomena, namely, new internal epistemic needs, new technes, new academic arrangements, new forms of scientific

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6 Ursula Klein, *Experiments, models, paper tools: Cultures of organic chemistry in the nineteenth century*, Stanford California Stanford University Press, 2003. This books shows how Berzelius paper formulae served many functions such as, the construction of a new classification of elements, acted as tools to work out ideas on paper with an impact on experimental set ups, as interpretative models of chemical reactions. Other paper formula systems deriving from Berzelius such as those of Kekule and Fischer also have a multifunctional character. Another important work on paper formula is: Ursula Klein (ed), *Tools and modes of representation in the laboratory sciences*, Dordrecht Boston London, Kluwer academic publishers, 2001. On 3D models see: Eric Francoeur, 'The forgotten tool: The design and use of molecular models', *Social Studies of Science*, 1997, 27: 7-40. Eric Francoeur, 'Molecular models and the articulation of structural constrains in chemistry', U Klein (ed), *Tools and modes of representation in the laboratory sciences*, Dordrecht, Boston, London. Kluwer Academic Publishers, 2001, pp. 95-116, and Soraya de Chadarevian, Nick Hopwood, *Models: The third dimension of science*, Stanford California, Stanford University Press, 2004.

7 This study not only proposes the existence of a latest visual form from molecular, but also a historical classification of all its forms (see later in this introduction and Chapter 1, subsection: *'The molecular imagery and cell biology: An historical overview of its visual forms and its relationship with cytology (the three ways of molecularisation)'*.

8 A change that also entails changes at the epistemological level.

9 Lorraine Daston and Peter Galison, *Objectivity*, 2007 New York, Zone Books, 2007. The concept of scientific selves refers to an array of ethical and moral codes and attitudes that are internalised and enacted by scientists and that results determinant for the practice of science at a given period. Different times favour the use of an array of particular ethical and moral codes for the pursuit of knowledge hence different times would have different types of scientific selves.

selves and new forms of organising principles, all relate to and could explain the development of the visual change in cell biology.

## THEMES AND QUESTIONS

Four axes of interrogation run throughout this dissertation as main organising themes. These are: imagery characterisation (what the images involved in the visual change are, what do they do, and how they got standardised), theoretical and historical location of the study (discussion of previous historical and theoretical works to which this study relates), connected developments (technological, socio-cultural and professional) and the framing of its consequences (the proposed self-referentiality of molecular imagery and its consequences for experimental practice).[10]

The first step this dissertation takes is to identify and characterise the images involved in the visual change that the discipline of cell biology has undergone during the period 1950s-2000s.[11] A comparative visual examination of past and present editions of cell biology textbooks reveals three main types of images at the centre of this visual change. Images of cells produced by optical microscopes, by electronic microscopes and images of molecular models of cells produced by instruments of a different nature to that of microscopes.[12] Images of an optical and an electronic origin are conceptualised in this study mostly as of one type only to highlight the fact that contrary to those of the molecular nature they are based on two key organising principles/metaphors: that of the microscopic image as an extension of naked eye observation, and that of the 'window into the invisible world.[13] For molecular imagery although these organising

10 This division is only operational and as such it may entail many themes that criss-cross boundaries.

11 The examination was first qualitative in the sense of recognising the different kind of images contained in textbooks then confirmed by a quantitative analysis. There are of course many different types of images in cell biology textbooks such as chart and diagrams. All images were divided in categories, (see chapter 1 for more details on all the types of images contained in cell biology textbooks).

12 The order optical, electronic and molecular corresponds to the chronological order as they appeared in cell biology. Changes in the other types of images are far less significant than those observed between microscopical and molecular images.

13 For the role of the metaphor of the 'window into the invisible' see: Bas van Fraassen, *Scientific representation: Paradoxes of perspective*, Oxford, Oxford University Press, 2008, pp.96. The third key

principles/metaphors are also at play, they are in need of extra justification, for they derive, as we will see later, from a complex process of translation of signs. In addition, to the eye extension based imagery this dissertation argues that the latest form of molecular imagery has an extra organising principle, albeit of a wider nature, that of 'the network' (discussed in Chapters 3 and 6).

One of the originalities of this study is to explore the similarities and dissimilarities between molecular images and the two others (optical and electronic) at three levels: signification, construction and standardisation. Starting with signification, this study compares the characteristics of each of these images with the three types of signs proposed by Charles Sanders Peirce (1839-1914), index, icons and symbols.[14] It compares the relation between optical, electronic or molecular images (signs) with the referent, that is the cell. By taking into account Peirce's point that the degree of convention, increases as we move from icons, through indexes, to symbols, this study reaches the following conclusions (Chapter 4). Optical images could be granted the category of icons, electron micrographs that of indexes and molecular images that of symbols.[15] Based on this comparison this study conceptualises the nature of the change observed in the visual history of cells (hinted at in Chapter 4) as one moving from an iconic to a symbolic modality.

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metaphor proposed by van Fraassen, that of 'engines of creation', (in the sense that they create new observable phenomena) applies to the three types of images discussed here.

14 James Hoopes (ed), *Peirce on signs: Writings on semiotic*, The University of North Caroline Press, 1991. Nathan Houser, Christian Kloesel (eds), *The essential Peirce* vol, I (1867-1893) & vol II (1893-1913). The Peirce edition project, Bloomington and Indianapolis, Indiana University Press, 1998. Roland Barthes, *Elements of semiology*, London: Jonathan Cape, 1967.

15 Indexical in the sense that the relationship between sign and referent is sensed as being almost physical The causal physicality is like an emergent property that results from putting a new image alongside another that has been previously granted a status of iconicity hence of authenticity; a strategy that relies on the continuity of vision argument: This dissertation argues that the composed image of fibroblasts, taken with an optical and an electronic microscope by Porter, et al. in 1945 (see Chapters 1 and 4) is the first type of image that had made that physical connection.

This association between each type of image and a particular sign, alongside the issue of transfer of 'traces' will serve us to explore two related issues.[16] On the one hand, how images of molecular culture build their authenticity for claims to reliable knowledge and on the other, how they do it with some independence from their content (see Chapter 4).

The capacity of scientific images in general and molecular images in particular to create meaning on their own is normally concealed from view. This should not surprise us since their meaning in science is largely attributed to their content, and their content is taken to be models, which in turn are taken as the visual component of theories.[17] Without denying the importance of this claim, this dissertation takes a different stance. In doing so, it exposes the intrinsic and relational capacity of molecular images to create trustable meaning to define the 'real' in cell biology.[18]

Regarding the issue of attainability of reliable knowledge throughout imagery production, this study builds on Martine Joly's ideas of the 'trace'. The 'trace' refers to the element of intimate association between image and eventuation (indexicality), which is typical of the resultant effect of photography-like images that end by transforming the

16 Joly for instance uses the example of x-ray images. See, Martine Joly, *Introduction a l'analyse de l'image*, Paris Nathan, 1993. Martine Joly, *L'image et les signes: Approche sémiologique de l'image*, Paris Nathan, 1994. Martine Joly, *L'image et son interprétation*, Paris, Nathan, 2002. Martine Joly, 'Les trois dimensions de l'image', *Sciences Humaines*. 2004, 43 : 10-13. The process of transfer of 'traces' of indexicality is explained immediately in what follows and with more detail in chapter 4, subsection 4.3 *'An alternative way to read the visual change: reading images as signs'*.

17 Theories are still highly valued despite the 'experimental turn'. By 'experimental turn' I refer to the 1980's change on focus from theory to experiment in philosophical studies of science. Ian Hacking, *Representing and intervening: Introductory topics in the philosophy of natural sciences*, Cambridge, Cambridge University Press, 1983. Building on Hacking's ideas a book that collects many interesting approaches to the issue is: Hans Radder (ed), *The philosophy of scientific experimentation*, Pittsburgh, University of Pittsburgh press, 2003. As Morgan and Morrison bluntly put it 'we use models as instruments to build theory'. Mary S Morgan, Mary, Margaret Morrison, *Models as mediators: Perspective on natural and social sciences*, Cambridge, Cambridge University Press, 1999, pp. 7. By intrinsic value of images I refer to their capacity to justify knowledge only by their condition of being images. This point, which is part of a central argument of this dissertation, will be extensively discussed in Chapter 4.

18 Of course the meaning of images is also, as Sturken and Cartwright suggest, the result of a complex interplay from producers interests, viewers identification with them and the social context of viewing. Marita Sturken, Lisa Cartwright, *Practices of looking: An introduction to visual culture*, Oxford, New York, Oxford University Press, 2001, pp.25-30, pp 45-47.

image into an icon.[19] This dissertation takes Joly's arguments further and argues that images of a molecular nature, despite the invisibility of their components (molecules), are taken to be referents themselves by a mechanism of transference of iconicity into the symbolic image. This is because their capacity to incorporate 'traces' of indexicality and also of iconicity in a kind chain mechanism that has been constructed historically (highlighted in Chapter 4).[20]

Related to the matter of trust in images as sources of reliable knowledge, there is a related issue that this dissertation considers worth reflecting on. That is the subordination of images to text, a widespread view among many scientists and philosophers for scientific images in general. Images are displayed, the argument runs, as a complementary strategy to reinforce and even embellish the epistemic point raised in the text. The intrinsic and relational role of images for the creation of worthy knowledge and their subordination to text remains unacknowledged because of the way they are portrayed in scientific and some historical accounts on the history of the discipline.[21] In the case of scientific accounts, the conception of images as subordinate to text goes hand in hand with the idea of 'constructive progress', a sort of teleological view that prioritises knowledge from different origins as complementary and building progressively towards a sort of predefined objective. When uncritically used by non-scientific scholars these accounts became what Shapin and Shaffer designated as the 'members' accounts'.[22] The combined picture resulting from both visions' 'constructive progress'[23] and 'members

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19 Joly argues that this transfer of 'traces' of indexicality is at the basis of medical imagery such as MRI scans and which results from its conventional component being erased. Martin Joly, 1994, 2002, op. cit.

20 All that said, it is important to recall that although images have some independence from what they contain, they became meaningful by being framed in discourses that relate them to other bodies of knowledge.

21 This type of account is typical of historical introductions on cell biology textbooks and articles see for example, Paul Nurse, 'The incredible life and times of biological cells', *Science*, 2000, 289:1711-16.

22 Stephen Shapin, Simon Shaffer, *Leviathan and the air pump: Hobbes, Boyle and the experimental life*, Princeton New Jersey, Princeton University Press, 1985, pp. 4-5.

23 'Constructive progress' is a term I designate to indicate the idea commonly held by scientists of different lines of inquiry contributing to the linear progress of a discipline. It entails the idea that disciplines contain from the outset a plan that it is sooner or later achieved. Constructive progress implicitly understands that if a discipline is conformed by two or more lines of inquiry, they complement, but the

account' not only creates a situation of neglect on the role of the intrinsic qualities of images to knowledge production, but it contributes to the portrayal of the entire issue of scientific imagery as unproblematic and as one devoid of tensions.

This dissertation opposes the view that images are subordinate to text in two ways. It proposes to look at images in themselves rather than at the models they may contain.[24] In addition, it proposes that both kinds of imageries, the microscopical and the molecular are involved in the making of different epistemic points that do not always act constructively and/or complement each other. This point will be sustained by showing the emergence and further development of the themes of 'signal transduction' and membrane 'embedded receptors' with signalling functions, two themes hinging almost exclusively on the new molecular imagery and that represents a clear disruption with previous knowledge in the discipline.[25]

Continuing with the aim of exploring similarities and dissimilarities between molecular images and the two others types, optical and electronic, the second level of this exploration deals with the process of their construction. All images are constructed, that is, they originate from a complex process of interpretation and translation of output data from instruments, a process that ends by transforming them into meaningful visual signs. Optical, electronic and molecular images are however the result of different processes of construction due in part to the nature of the instruments used to obtain them. As anticipated by the work of Knorr Cetina and Altman (discussed in Chapter 4) images of a molecular nature are constructed through a process of interpretation of the traces left 'by molecules' in test tubes.[26] This study takes their view further by showing how these 'molecular traces' have been used to create a new visual form of molecular culture and

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latest and more sophisticated one is closer to how the system 'really' works. Disciplines thus function as systems that are always surpassing whatever had gone before.

24 This argument is substantiated by the conception on the making of images by the authors of MBC, especially Keith Roberts (see later what follows in this introduction and Chapter 3).

25 These two subject areas are presented later in this introduction and discussed more in depth in Chapter 1.

26 Karin Knorr-Cetina, Klaus Amann, 'Image dissection in natural scientific Inquiry'. *Science Technology & Human Values*. 1990, 15: 259-83.

by so doing, extended their reach into defining cellular anatomy at a functional level (Chapters 1 and 4).

The third level of our exploration on the similarities and dissimilarities between molecular images and the two others types optical and electronic is that of the process of standardisation of molecular imagery. The focus is on establishing how the process by which molecular imagery was rendered trustable for their consumers, students and established researchers worked. The production of molecular imagery is investigated through interviews with the authors of MBC, a key textbook from molecular culture, which proved to be essential for the imagery change in the discipline (see later on textbooks, and in Chapter 3).

The different visual forms of molecular imagery in its relation to cell biology.

The process of growth of molecular culture in biology has attracted the attention of many scholars. Important works have been produced on the expansion of this culture under the rubrics of 'molecularisation' and 'molecular vision of life'.[27] In a similar vein, a sort of periodisation was proposed for this 'progressive colonisation' of biology by molecular culture.[28] The historian of molecular biology, Abir Am, for example, has

27 Molecularisation is a descriptive concept referring to the conceptualisation of all life phenomena as having a molecular base. In the particular case of cell biology, conceptualising all cell functions as being produced by an internal network of interacting molecules. Molecularisation has many connections with other related terms such as Kay's 'the molecular vision of life', see Lily E Kay, *The molecular vision of life: Caltech, The Rockefeller foundation and the rise of the new biology*, Oxford New York, Oxford University Press, 1993, and with the concept of 'molecularising' as defined in Soraya De Chadarevian and Hermke Kamminga, *Molecularizing biology and medicine: New practices and alliances 1910s-1970s,* Amsterdam, London Harwood academic publishers, 1998. The connections of my concept with theirs is due to the fact that the molecularisation of biology apart from entailing a visual shift (the central argument of my thesis) also entails new links among the different factors involved in its development such as scientists, funding bodies, governmental policies, scientific institutions, as well as, new laboratory and managerial practices. The following apart from the two already mentioned are some of the works that widely cover different aspects of the history of molecular biology in particular and molecularisation in general: Hudson F Judson, *The eight day of creation: Makers of the revolution in biology,* London, Penguin Books, 1979. Michel Morange, *A history of molecular biology*, Harvard University Press, Cambridge Massachusetts & London England, 1998. Susan Wright, *Molecular politics: Developing American and British regulatory policies for genetic engineering, 1972-1982,* Chicago, Chicago University Press, 1994. Pnina G Abir-Am, The Politics of macromolecules: Molecular biologists, biochemists, and rhetoric, *OSIRIS*, 1992, 7: 164-191.

28 Pnina G Abir-Am, 'The molecular transformation of twentieth-century biology', in J Kriege and D Pestre (eds), *Companion to science in the twentieth century*, London, New York, Routledge, 2003, pp 495-563.

identified three phases in the molecular transformation of biology that she dubbed as 'phases of transdisciplinary stabilisation': The first phase, lead by biochemistry is that of metabolic pathways running from 1900 to 1937. The second one, that of the early molecular biology running from 1938 to 1973. And finally, the third phase, also lead by molecular biology, characterised by the development of recombinant DNA technology, which began in 1974 and runs to the present. None of the works mentioned however, dwells on the manifestation and characteristics of the latest form of molecular imagery in cell biology, a key emerging theme that this dissertation explore and assesses (as shown in Chapter 1).[29]

This dissertation not only identifies and characterises the new visual forms from molecular culture, with its main component, that of signal transduction and membrane embedded receptors with a potential signalling function, but also creates a historical classification of the different expressions of molecular culture where this latest expression fits (see Chapter 1).[30] Molecular culture has displayed historically many visual expressions all having different degrees of connection with cell biology well before the 1980s.[31] The first type of visual forms from molecular culture to emerge (first-generation models) was that of paper formula, an on paper depiction using letters to indicate the atomic composition of molecules and lines interconnecting them to indicate their bonding.[32] Paper formula emerged by the mid 19th century; they are of diverse types and are still in use nowadays. From the mid 1930s onwards, three new types of molecular-based visual forms arose (second-generation models): biochemical models of metabolic cycles, three dimensional models (3D models) of proteins and 3D molecular biology models such as DNA double helix, protein synthesis, DNA replication and the operon

29 Abir Am's work for instance, although very relevant on the characterisation of epistemic changes on the process of molecularisation and on the details of their protagonists and conditions of emergence does not deal with the imagery of molecular culture that those phases brought about.

30 Signal transduction imagery refers to images of models set to explain all the intracellular molecular interactions (protein-protein interactions) occurring inside cells after a receptor in its surface interacts with its external target. Membrane embedded receptors refers to images presenting molecular designs of complex proteins arrangements embedded in the cell membrane that change shape and incorporate other proteins after the interaction with an external substrate and have a signalling function.

31 This classification of the different expressions of molecular culture in three main forms is original to this dissertation (see Chapter 1).

32 Klein, 2001, op. cit. Klein, 2003, op. cit.

model of gene regulation. This second type of visual forms from biochemistry and molecular biology (second-generation) show a higher reliance on cellular themes (metabolism, cell division, secretion) than those from the first-generation (paper formula).[33] Nevertheless, it is argued here that despite this closer reliance, images of biochemical and molecular biology models did not overlap with the images of cells produced by microscopical culture. In effect, as shown in Chapter 1 both kinds of imageries, the microscopical and the molecular, were located with a few exceptions in different chapters in cell biology textbooks form the 1960s and 1970s. Moreover, the first and the second forms of imagery from molecular culture although important, were never sufficiently significant in number to compete with the ones produced by microscopes in cell biology textbooks during that time (shown in Chapter 2). Finally, the third visual form of molecular imagery comprises mainly that of 'signal transduction' and membrane embedded receptors, a type of visual expression including complex arrangements of interacting proteins that emerged by the late 1970s, and was firmly established by the mid 1980s.[34] This dissertation argues that it is this latest visual form of molecular imagery that is responsible for the visual change in cell biology.

The latest visual form from molecular culture began to manifest itself in different media such as scientific articles and textbooks from the mid 1970s onwards. It began to compete in these media for representational space with the images of the microscopical tradition from the 1980s (shown by the quantitative work presented in Chapters 2 and 3).

The role of textbooks for the expansion of molecular imagery.

Textbooks have been given prominence in this dissertation in order to study the visual change, chiefly because of their more permanent nature as sources of knowledge when compared with scientific articles (Chapter 2). Besides, textbooks were essential for

33 Key for knowing how the metabolic pathway that produces energy inside the mitochondria of cells (oxidative phosphorylation) worked, was the imagery provided by the electron microscope. For more details see Bechtel, 2006, op. cit, pp. 215-19.

34 This expression also includes the following forms: a) models of protein synthesis and protein modification associated with cellular components such as the rough endoplasmic reticulum, b) membrane associated protein channels involved in internal and external ionic or macromolecular transport. (see Chapter 1 for more details).

the process of the molecularisation of cell biology (the growth of molecular culture in cell biology). By the late 1970s, the creation of a textbook in cell biology from a molecular perspective was essential to more efficiently link the sites of production of knowledge (laboratories) with the sites of production of newcomers to the profession (lecture rooms at universities).[35]

The first cell biology textbook produced with that purpose in mind and that began to display the latest form of molecular imagery was *Molecular Biology of the Cell* (MBC), which was first published in 1983 and has a total of five editions up to present.[36] MBC is the textbook targeted for analysis in this dissertation for it is the main printed media, apart from the Journal *Scientific American*, where the visual change began to unfold. As hinted in Chapter 3, MBC was produced by a set of authors led by James Watson, for whom the appliance of the molecular paradigm was essential to renew the face of what they perceived as an otherwise 'too anatomical' and 'too factual' cell biology (gathered from the interviews of the authors in Chapter 3). In many ways MBC can be considered as a watershed in the discipline. This, not only because, as I will show in Chapter 3 it exhibits novelty in its making, but more importantly because MBC was the main medium that conveyed the latest visual form of molecularisation to different audiences, namely students and established scientists. All that being said, the molecular imagery displayed in MBC wouldn't make too much sense on its own. Hence the necessity to compare with the textbook *General Cytology*, renamed Cell Biology (CB) in its edition of 1970, which was first published in English in 1948 (original in Spanish, 1946) and had seven more editions under different titles and with different authors.[37]

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35 This began to be imperative firstly because at the time many laboratories were already applying the new 'techne' of genetic engineering in eukaryotic cells and secondly because it seemed to be essential for the successful social reproduction of the burgeoning molecular culture, especially when the economic potential of such techne became apparent.

36 Bruce Alberts, Dennis Bray, Julian Lewis, Martin Raff, Keith Roberts, James D Watson, *Molecular biology of the cell*, New York, London, Garland publishing, Inc, 1983, 1989, 1994. Bruce Alberts, Alexander Johnson, Julian Lewis, Martin Raff, Keith Roberts, Peter Walter, *Molecular biology of the cell*. New York: Garland Publishing, 2002, 2008.

37 CB is used to refer to the different editions of Eduardo D P De Robertis, Wicktor W Nowinski, Francisco A Saez, General cytology, Philadelphia, Saunders Company Philadelphia, 1948, 1954, 1965. Eduardo D P De Robertis, Francisco Saez. Eduardo M F De Robertis, (Jr), *Cell biology*, Philadelphia, Saunders Company, 1975. Eduardo D P De Robertis, Eduardo M F De Robertis, *Cell and molecular biology* (CMB), Philadelphia, Lea & Febiger, 1980, 1987. Whereas my analysis includes all the editions of

What make CB, an excellent textbook to compare with MBC is that it belongs to the microscopical tradition and that its editions overlaped for a while with those of MBC. The editions of 1948, 1954, 1965, 1975 and 1980 editions preceded the first edition of MBC (1983) and that of 1987, edition followed it. Two additional reasons, shared by GC and MBC, make them suitable sources for a comparative analysis. Firstly, it is possible to recognise common themes running through the different chapters from all the editions assessed of both textbooks (see Chapter 2). Secondly, CB and MBC were in their times two of the most popular textbooks for university students of the biosciences not only in the USA and Britain, but also all over the world as the translation to the different languages of both treatises suggests.

One key topic that this study identifies when exploring the production of MBC is the innovative role played by the textbook in the standardisation of the latest form of molecular imagery (insights in Chapter 3). Rather than based on the classical procedure of a circle of experts producing images and consulting with a few other experts from whom they could accept some concrete images, the standardisation of the latest form of molecular imagery was based on the establishment of a complex networked process of participation and consultation between the authors, scientists from all over the world and university students that warranted its acceptance (shown in Chapter 3). This degree of network connectivity was an alien practice for the 'scientific selves' makers of the 'eye-based' imagery. It is argued here that this network functioning, created the perfect 'virtual witnessing' scenario for the standardisation of the new non-eye based imagery, for it cancelled out the emergence of possible alternative readings among its users.[38]

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MBC, only six out of the eight editions published (1948, 1960, 1965, 1975, 1980 and 1987) of CB were surveyed, since those of 1954 and 1970 were not available. *General Cytology* (GC) is used interchangeably with De Robertis' et al to describe all the editions.

38 'Virtual witnessing' is a term proposed by Shapin and Shaffer, referring to the staged experiments of Robert Boyle with the air pump in the 1660s. They served to create a condition in a reading audience that accepted the observations and outcomes derived from those experiments and simultaneously to accept the conditions of its production. Shapin, 1985, op. cit., pp. 60-5.

Theoretical and historical location of this study.

There are many meaningful and relevant works apart from the ones already mentioned that this dissertation relates to and derives inspiration from. Two main lines of inquiry are distinguishable among them: studies on the history of the microscopical tradition and studies on scientific representation.[39]

The microscopical tradition was pivotal for the emergence and final establishment of cell theory (1840s-1930s) as well as further developments such as the conceptual shift from cells as mere structures, to cells as structures with associated biochemical functions that took place between the 1940s and 1960s.

It is important to note two points concerning previous historical studies on cell biology, the first is that they stop at the 1970s, and the second is that their main focus is epistemological. This study is different in that respect, in that it looks at a period of the history of cell biology that has not yet been covered, that from the late 1970s, onwards, and in that it describes a change at the level of its imagery rather than just epistemologically. Moreover, this study conceptualises the molecular imagery as representing a deep discontinuity with microscopical imagery (discussed in Chapter 1). Arguing for a discontinuity in visual expression in cell biology also involves arguing for a limitation of the 'continuity of nature' argument.[40] This principle, which is endorsed by molecular cell biologists, supports as unproblematic the possibility to connect in a continuum images of visible entities to images of invisible ones. It is argued here that attempts to establish such a continuum from images of cells obtained with an optical

39 Since for both lines of inquiry the amount of works is immense, the focus of this dissertation is selective. In this case I have choosen to focus only on those that deal with the key issues that relate closely to the interests of this study. It has to be mentioned that many studies are hybrids between the two categories.

40 The continuity of nature argument (also known as the continuity of vision argument) is a philosophical argument for scientific realism. It holds that entities existing in the world are in a smooth continuum, that there is no divisive point between the observable and the unobservable. In other words that there is an ontological continuity from what we see to what we cannot see. The philosopher Grover Maxwell, who first developed the argument, claimed that all entities are observable under suitable circumstances by using the proper instruments like a magnifier, an optical microscope, and so forth. Grover Maxwell, 'The ontological status of theoretical entities', in H Feigl, G Maxwell G (eds), *Scientific explanation, space and time*, vol 3 of the Minnesota Studies in the Philosophy of Science, Minneapolis, University of Minnesota Press, 1962.

microscope, passing through those obtained with the electron microscope, to those obtained with instruments and techniques of a different nature has its limits. As Luc Pauwels points out justification problems arise when 'the referent is postulated' and the evidence for its existence is reached through indirect representation.[41]

Whilst being aware that the continuity of vision argument could be abandoned even at the level of optical images, this study sets the limits for it for the optical microscope.[42] That said, it is important to indicate that even if this study takes electronic images as different to optical ones there are a number of respects in which they overlap. The construction of the instruments from which they originate is based on the same conceptual idea of using lenses, albeit of a different physical nature, to extend the observation being made with the naked eye.[43] To this it should be added that the observational aim for both instruments, is to preserve as far as possible the structure of cells intact in order to be able to reach epistemic conclusions on their structure and behaviour. Molecular images are of a completely different class to those of both microscopes. In the first place, the two main technologies that produce these images are by and large based on a complete 'destruction' of the referent as such (cells are lysed).[44] Secondly, as discussed in Chapter 1, the visual outputs from these techniques are, as Knorr-Cettina put it, 'traces' (dots in radiograms) of reactions occurring in a test tube that are subsequently translated into another type of image.

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41 Pauwells, 2006, op. cit., pp. 9.

42 van Fraassen, 2008, op. cit. van-Fraassen distinguishes between observations, and detections. Whilst the firsts are non-mediated by instruments the second class are. He takes optical microscopy to be an instrument mediated phenomena, hence as a detection, as opposed to direct eye-mediated perception pp. 93. I take optical images, even if they are instrument mediated, as observations and reserve the category of electronic and molecular images as detections.

43 Both instruments are based on the use of different regions of the light spectra and the use of different types of lenses. Concerning structural preservation, this has been a controversial issue on the standardisation of electron microscopy imagery. See for instance Harold Hillman and Peter Sartory, *The living cell: A re-examination of its fine structure*, London, Packard Publishing Limited, 1980.

44 The two main techniques used two describe interacting proteins in cells are known as Immunoprecipitation/Western blotting (IP/WB) and two hybrid system.

A key theme that this dissertation touches upon is that of scientific representation in science and cell biology in particular.[45] Several issues around the picturability of the invisible that are of interest for this dissertation are raised in Arabatzis' book on electrons.[46] Arabatzis argues that historically speaking, electrons have been very elusive entities because they have displayed different features under different experimental conditions. This elusiveness also lies, in Arabatzis' view, in chemistry physics, that clashing over the creation of their image. Creating images for the electron was related to the different epistemic needs that each of these disciplines had to explain different phenomena. So, while the chemists wanted to explain chemical combination, physicists wanted to know about the role of electrons in the phenomena of atomic spectra and cathode rays.[47] The result was the existence of two contrasting images that were mutually compatible, but that did not always corresponded with each other. A similar conclusion to that of Arabatzis on electrons is arrived at in this study concerning the production of knowledge on cells by the microscopical and molecular cultures of image production in cell biology.

Continuing with the depiction of the invisible, the other type of historical approaches that this dissertation engages with are those that highlight instances relevant for the growth of molecular imagery inside cell biology. Cambrosio and Keating's analysis on the deployment of a new non-visual technique in immunology, called flow cytometry is illuminating because it is based, like the images described in this study, on the translation of one kind of output image into another of a different nature.[48] The instrument that the authors assess is called a flow cytometer, which takes measurements of the number of cells, manipulates them with the aid of complex software to subsequently translate this 'raw' data into an optical event of a different type, a plot

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45 The literature here is immense, so my focus once again is selective and point towards particular themes (see what follows).

46 Theodore Arabatzis, *Representing electrons: A biographical approach to theoretical entities*, (Chicago, London, The University of Chicago Press, 2006.

47 Arabatzis, 2006, op. cit., pp. 14 and pp. 190.

48 Alberto Cambrosio, Peter Keating, 'Of lymphocytes and pixels: The techno-visual production of cell populations'. *Studies on History Philosophy of Biology. & Biomedical Sciences*, 2000, 31: 233-70.

image, on a computer.[49] This dissertation takes a different view though on the type of constructed images analysed by Cambrosio and Keating. It argues that firstly, although they distinguish two different meanings for 'representation', one to denote description and the other to denote theory, they use the term as if 'representing' cell populations is attainable.[50] The second objection to this study concerns their categorisation of the digitally produced plots of cell populations as icons of human health.[51] These plots look more like symbols than icons, for they do not harbour any relationship of resemblance to the 'real lymphocytes' (referent/object) as they look under an optical microscope.

The work that emerges as central for this dissertation, is that of Hans-Jörg Rheinberger's on 'epistemic things'.[52] Since epistemic things could be as varied as physical structures or processes that constitutes the objects of enquiry, such as biochemical reactions and biological functions, it is quite reasonable in fact to think of the networks of interacting proteins (signal transduction) as epistemic things. There is one aspect however, in which epistemic things substantially differ from the images of molecular culture this dissertation describes. Epistemic things in Rheinberger's view are material entities resulting from experiments which are not necessarily related to 'referentiality' at least not to the kind of referentiality at play for visible entities. This point, flagged up by David Bloor is one of the most controversial issues arising in Rheinberger's work and is the one where my work departs from it; although not fully into Bloor's direction either.[53] In Rheinberger's view referentiality is not a condition for epistemic things to exist. In his own words, 'epistemic reference is suppositional', meaning that although epistemic things refer to something, 'its precise meaning remains elusive'.[54] The importance of epistemic things resides in their potentiality to become

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49 Cambrosio, et al. 2000, op. cit., pp. 239.

50 Ibid, pp. 235.

51 Ibid, pp. 263.

52 Hans-Jörg Rheinberger, *Towards a history of epistemic things: Synthetizing proteins in the test tube*, Stanford, California, Stanford University Press, 1997.

53 David Bloor, 'Towards a sociology of epistemic things', *Perspectives on science*, 2005, 13: 285-312.

54 Hans-Jörg Rheinberger, A reply to David Bloor: "Toward a sociology of epistemic things", *Perspectives on Science*, 2005, 13: 406-10.

technical objects, that is, objects with which new experimental networks could be created. His work entails the creation of 'spaces of representation' born from experimental conditions where invisible entities detected not through a microscope but through their traces became epistemic things. For this dissertation however, referentiality matters, for it is on this very possibility that the images discussed in this study differentiate from each other (see Chapter 4). In other words, this study clearly differentiates 'representations' with referents from those that do not have one. Moreover, it does so by arguing that it is more appropriate to use the concept of 'presentation' when picturing the invisible than 'representation'.[55] Another point of divergence between Rheinberger's position and the one adopted in this study is that whilst Rheinberger's identifies the creation of symbolic forms as a material process rather than a linguistic one, I posit this creation on the intrinsic and relational capacity of images to account for authenticity.[56] One point of convergence between this study and that of Rheinberger's is that both see the importance of epistemic things or molecular imagery to create new experimental networks. Nevertheless, what this study sees as different is that these new experimental networks are creating a condition of self-referentiality among images, a topic that remains unattended in Rheinberger's work (see later in this introduction and Chapter 6).[57]

Connected developments:

This dissertation identifies four developments to which this imagery change in cell biology relates to and that could eventually explain its conditions of emergence. They are, firstly, the 'internal' epistemic need of molecular biologists to extend the molecular paradigm to the whole of the biosciences and in particular to eukaryotic cell biology. Secondly, the emergence of new technologies. Thirdly, the emergence of a distinctive

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55 Presentation results a better term to indicate that picturability of the invisible, for it defines better a free act of creation not related to mimesis or copy of a referent (since this one is suppositional). See Pauwells, 2006, op. cit. And later discussion in Chapter 4.

56 Rheinberger, 2005, op. cit., pp. 408.

57 Creating conditions where not only the visible invisible divide conflates but conditions where to determine the ontological status of invisible entities is always postponed (referred) or *tout-court* don't matter.

type of 'scientific self' associated with the ethos of molecular culture and opposed to that of the microscopical culture.[58] And fourthly, changes in academia oriented to mirror and follow wider societal settings.

A) Internal epistemic needs

The key 'internal' initial development for this visual change resides in the necessity to validate the universality of the dogma of molecular biology as developed in previous centuries on bacteria and viruses.[59] It became essential for molecular biologists to show that the knowledge that molecular biology achieved on prokaryotes, namely DNA duplication, protein synthesis and the operon model for gene regulation also applied to eukaryotes. Equally important for this was the prospect of finally delivering the long time dreamed 'productive forms of intervention' on life.[60] It has been argued, that these 'needs' for universalisation and intervention began to unfold by the 1930s when molecular biology began to take form as a discipline.[61] After many years, the basis for the evaluation of the universality of genetic mechanisms became finally feasible with the emergence of DNA recombination and genetic engineering in the late 1970s early 1980s. Their emergence allowed for the expansion of the molecular paradigm inside cell biology and with this the process of redefinition of cellular themes in molecular terms. This dissertation argues for a pivotal role played by molecular imagery for this process to succeed.

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58 Daston, 2007, op. cit. (see reference number 9 for the meaning of the concept of scientific selves).

59 Morange has portrayed the period (1972-1980) as one in which an 'operational control' became available to apply the 'conceptual tools for analysing biological phenomena that were forged between the 1940s and late 1960s. Morange, 1998, op, cit., pp. 2. See also Michel Morange, 'La grande collaboration', in 'Les mousquetaires de la nouvelle biologie: Monod, Jacob et Lwoff'. *Pour la Science*, 2002, 10: 3-96, pp 35.

60 Productive forms of intervention refers to the ideal already envisaged in the 1930s of engineering life to correct constitutive faults and/or to produce substances with therapeutic potential. See Kay, 1993, op. cit.

61 Aims that were linked to the eugenics ideals of intervening on 'undesirable' aspects of a society's members. Kay, 1993, op. cit.

B) New technologies

The occurrence of new technologies such as genetic engineering and new forms of immunoanalysis to study interacting proteins in cell homogenates was central for the process of molecularisation and for the development of the new molecular imagery in cell biology.[62] Brief technical details of some of these techniques and their epistemic aims are given in Chapter 1. Here it suffices to mention that from the mid 1970's onwards there was a re-configuration of old and new technologies that allowed the creation of new visual outputs that in turn called for new ways of interpretation and translation.

This dissertation shows, much in line with Maria Trumpler's work on neurobiology models that particular technologies are associated with particular forms of visual representation.[63] Trumpler describes how the same phenomenon of the cellular transmission of electrical impulses underwent a representational conversion from 'sodium conductance', expressed as a diagrammatic electrical model to one of a 'protein channel', expressed as globular molecules embedded in membranes depending on the use of two different techniques. Whilst Trumpler speaks of substitution of models by the emergence of new technologies, this dissertation speaks about survival of previous forms (microscopical) and competition for representational space.

C) Scientific selves and cultures of image and knowledge production

This study attempt to shows that equally important for the molecularisation of cell biology as for the emergence of the latest form of molecular imagery, was the emergence of new forms of scientific selves and working practices for image production in cell biology. Although openly welcomed by the scientific selves of the microscopical culture during the 1960s and 1970s, (Chapter 2) the molecularisation of cell biology was only partially accomplished by them. Its full development was achieved by a new generation

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62 Genetic engineering refers to the capacity to cut and paste DNA from different origins. It allowed to intervene in life phenomena and to test the function of genes in different cellular contexts. The new forms of immunoanalyis refers to the combined application of antibody mediated immunoprecipitation of specific proteins from cell homogenates used in conjunction with two other techniques (electrophoresis and western blotting) where interacting proteins could be detected and subsequently be identified. This new from of immunoanalysis also includes in the study of phosphorylated proteins, which would define its interactions with other proteins.

63 Maria Trumpler, 'Converging images: Techniques of intervention and forms of representation of sodium-channel proteins in nerve cell membranes', *Journal of the History of Biology*, 1997, 30: 55-89.

of researchers that entered cell biology at that time in possession of the promising interventionist technique of DNA recombinant technology. But that was not all, they also possessed a new set of moral attitudes based on a new conception of entrepreneurship and willingness to try more 'flexible' practices to achieve the expansion of the molecular paradigm inside academic settings and a wider society that favoured these types of attitudes. In effect deep transformations began to take place in academia from the early 1960s, a process that has been incorporating many other elements such as new working practices from the private sector (see Chapters 5 and 6).

Shapin's recent book on the transformations on the scientific establishment in the US throughout the Second World War period and beyond is highly informative on this regard.[64] The period between the1950s and 1960s in Shapin's view was determinant for the transformation of science, 'from science as a calling to science as a job'.[65] He argues that the growing interest from the US national government in promoting the development of industrial like arrangements in academia had the effect of producing scientific entrepreneurs that began to have ambitions for wealth as any other type of worker. This dissertation takes the view that the visual change in cell biology also owes to the kind of wider societal and academic transformations deriving from the ones described by Shapin. It proposes that the transition from rigid production patterns in industry (Fordism) towards the more flexible patterns of production (Flexible specialisation) facilitated the emergence of a new type of cell biologist (see Chapter 6).[66] As discussed in Chapter 5, Harvard in the late 1950s and later Cold Spring Harbour (CSH) in the early 1970s were

64 Steven Shapin, *The scientific life: A moral history of a late modern vocation*, Chicago, The University of Chicago Press, 2008. Shapin builds his arguments on the lecture, 'Science as vocation', given by Max Weber, a key figure for the conformation of sociology as a discipline, in 1917, concerning working practices in German and American universities. Although controversial in some of its conclusions, Shapin's main arguments on the transformation of the scientific establishment in the US during the Second World war period and beyond, it remains a good guidance to assess the change in cell biology from a microscopic based culture into a molecular based one.

65 Shapin, 2008, op. cit. He means a science practiced as any other job, sometimes even as an obligation, with not passionate specialists as seen in previous times.

66 David Harvey, *The condition of postmodernity: An inquiry into the origins of cultural change,* Cambridge Massachusetts, Oxford UK, Blackwell publishers, 1990.

the academic places where James Watson, the main promoter of MBC, nurtured his skills as a scientific self of molecularisation.[67]

As hinted above and developed in Chapter 5 the molecularisation of cell biology was enacted by a different type of scientist. Whilst traditional cell biologists, belonging to the microscopical tradition such as Eduardo De Robertis, took science overwhelmingly as a vocation, almost as a sacred profession set well apart from other enterprises, the new generation of molecular biologists such as the authors of MBC, that began working on cellular themes by the mid 1970s took it instead as a profession, one that contained, just as any other profession, 'ambition and moral ordinariness'.[68] What is important to retain here is that for these different types of scientists, microscopists and molecularists what was meant by 'seeing' (practices of seeing) was different. Equipped with new techniques and new expertise, they changed the underlying culture of cell biology from one based on microscopical skills to one based on a combination of indirect techniques, hence more flexible ways, to create images of cells. For the new molecular biologists turned cell biologists there was more than just 'magnification' to describe cellular events. What is remarkable is that for the description of these cellular events as for their working practices the idea of a 'network' began to act as a key organising principle (see above in this Introduction and Chapters 3 and 6).

Expanding on the issue of scientific selves and practices of viewing, this dissertation has immensely benefited from Daston and Galison's latest work on objectivity.[69] The authors propose that what counts and/or prevails as objective knowledge in a discipline, 'epistemic virtues', depends on a set of moral codes and attitudes enacted by scientists, all of a historically dependent nature.[70] The epistemic

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67 Paul Doty 'Watson at Harvard (1956-1976)', in J Inglis, J Sambrook, J Witkowski, (eds), *Inspiring science: Jim Watson and the age of DNA*. Cold Spring Harbour, New York, Cold Spring Harbor Laboratory, 2003.

68 Shapin, 2008, op. cit., pp. 218.

69 Daston , 2007, op. cit.

70 Ibid. Epistemic virtues refers to what a correct depiction is expected to look like for those who produce it for a given historical period (see discussion in Chapter 4).

virtues identified by Daston and Galison are 'Truth to nature', 'Mechanical Objectivity' 'Trained Judgement', and 'Hybrid Practices'.[71] 'Truth to Nature' runs from the late 17th to the mid 19th century and is characterised by the selection of images representing ideal types, an object found in nature but idealised as a universal form. To 'Truth to Nature' follows, 'Mechanical Objectivity', which runs from the mid 19th century to the present day. Mechanical Objectivity refers mainly but not exclusively to photography, a practice viewed as an automatism aimed to prevent scientists' 'subjective' intervention. From 'Mechanical Objectivity' follows 'Trained Judgement', running from circa the mid 20th century to the present, an attitude that allows for interpretation and an expression of artistic (unconscious and intuitive) elements back into science.[72] What is more, with 'Trained Judgement' a new kind of pedagogy arose, one that would become very successful in forming self-assured 'trained experts' in the recognition of particular patterns in the representation of phenomena (e.g. Magnetic Resonance Imaging). Finally, the more recent epistemic virtue to emerge (in the late 20th century), that of 'Hybrid Practices', is characterised by a fusion of artifactual and natural elements resulting in practices where making and seeing are deeply entwined. The scientific self that constructs the imagery that characterises 'hybrid practices', the authors argue, combines the practices and values of scientist, engineer, entrepreneur and artist in a new light. As we will see in Chapters 3 and 5 these are many of the epistemic virtues possessed by the scientific selves that lead to the molecularisation of cell biology from the mid to late 1970s.[73] Building on previous ideas on the intrinsic capacity of images to produce meaning and Daston and Galison's ideas, this study argues that images displaying molecular interactions play the same role as exemplars for objectivity as photography did during 'Mechanical Objectivity'. The scientific selves of the microscopical and the molecular tradition are explored through the figures of Eduardo De Robertis and James D Watson respectively (see Chapter 5).

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71 Daston, 2007, op. cit., 'Truth-to nature' is discussed in Chapter II Pgs 55-113, 'Mechanical objectivity' in Chapter III Pgs 115-190, 'Trained judgement' in Chapter VI Pgs 309-361 and 'Hybrid Practices' as 'Representation to Presentation' in chapter VII Pgs 363-415. Unlike the authors who do not explicitly define 'Hybrid Practices' as an epistemic virtue, I choose to do so, because in my view this is an obvious case.

72 Ibid. pp. 370.

73 Ibid. pp. 381.

When exploring the microscopical and molecular cultures in cell biology this dissertation finds many parallels with the findings of Peter Galison in *Image and Logic.*[74] Firstly, because of his emphasis on the role of different cultural practices in the building of physics, a discipline that like cell biology deals with the invisible. Secondly, because it considers a vast panoply of factors playing a role in the practice of physics that changed from individual craftsmanship, typical of the late 19th century, towards a complex network of researchers each possessing different kinds of skills and approaches. In the case of cell biology, as in physics, we are facing the existence of two different epistemic cultures, each driven by a different set of practices and beliefs of what constitutes knowledge on cells alongside some organising principles that guide its research.

The idea of 'a window on the invisible world' (viewed as a metaphor by van Fraassen) alongside that of microscopic observations as 'extensions of naked eye observations' acted as key organising principles for microscopical inquiry.[75] Both have shown to be essential from around the 1660s when the first microscopic observations were made.[76] They continued to have an important value during the consolidation of cell theory between the 1860s and 1930s and during the consolidation of electronic microscopy in the 1940s and 1960s. When molecular culture entered cell biology in the mid to late 1970s (the third wave of molecularisation), even if its experimental technology was not based on lenses, its corresponding visual form (third-generation), chiefly that of signal transduction processes was to keep relying on both organising principles. It did so, by using implicitly the continuity of vision argument. Something else however began to emerge as a consequence of the relentless grow of these visual descriptions of interacting proteins, the idea of the network as an organising principle itself. Networked molecular interactions in signal transduction processes attempted to explain the way cells function. Maps of networked interactions among proteins would

74 Peter Galison, *Image and logic: A material culture of microphysics*, Chicago, London, University of Chicago Press, 1997.

75 van Fraassen, 2008, op. cit., pp. 96-7.

76 Hughes, 1959, op, cit. Harris, 1999, op, cit.

conform a catalogue for different cell behaviours such as growth, differentiation and death. This dissertation explores and discusses the limits of extending the 'continuity of vision' argument on this last visual expression of molecular culture (see Chapter 6).

A common assumption is that while the main role of microscopical culture has been that of viewing a cell under a microscope to describe its anatomy, the main role of molecular culture has been that of describing cell function. Although there is some truth to this assumption, this dissertation argues that the most important distinction between both cultures is of a different nature. It resides in what both cultures meant by 'seeing'. Whereas microscopical culture prioritises 'seeing' as viewing through a microscope, as an act of 'witnessing' through the eyes to produce knowledge on cells, molecular culture does prioritises 'seeing' as 'making' and 'intervention', as opposed to 'witnessing', much in line with the characteristics that Daston and Galison propose for the epistemic virtue of 'hybrid practices'.[77]

Framing the consequences of the visual change.

Based on Baudrillard's ideas on simulation and hypereality this study has also a contribution to make (as discussed in Chapter 6) about the putative consequences of this imagery change in cell biology.[78] Baudrillard proposes that 20th century Western societies are organised around the idea of consumption of images rather than commodities. As a consequence of this, the difference between referent and its representation disappears and a condition is established, one in which the real is substituted by the hyperreal. Social reality is constructed through simulation and those simulations; models are taken as reality itself.

Building on Baudrillard's ideas on hyperreality it is proposed here that the impressive growth of molecular imagery in the last 30 years in cell biology, in other words, the visual change from iconic to symbolic forms of expression, has produced a network of images, a self-contained imagery that risks of becoming self-referential. One that not only

77 Daston, 2007, op. cit.

78 Jean Baudrillard, *Simulacres et simulation*, Paris, Galilée, 1981. Jean Baudrillard, *L'echange impossible*. Paris, Galilée, 1999. Jean Baudrillard, *Symbolic exchange and death*, London, Sage Publications, 1993.

has created a condition of signs referring to each other in an almost endless way, but one that remains apart from microscopic imagery. This condition of 'hypereality' that values modelisation over microscopical observations is at the basis of what some cell biologists perceive as a neglect of the cellular model.[79]

The trust in the reliability of images of the invisible, their potential to slip into the 'unreal' and thus lose their explanatory power seems to be a recurrent theme in the history of biology, one that have been highlighted by studies that moved beyond the amalgamated narratives of the 'members' account' and 'constructive progress'. The work by Cambrosio et al on the German immunologist Paul Ehrlich's imagery on antibodies in the 1900s is illuminating at this respect.[80] The epistemic validity of Ehrlich's depictions, designed to conceptualise processes occurring in blood in test tubes, such as agglutination and haemolysis, was vigorously contested by the French immunologist Jules Bordet. Bordet viewed Ehrlich depictions as 'illusory representations' that could deviate the practice of science from its pursuit of 'objective experimentation'. This is not a trivial point, especially in light of a recent work by Breidbach that shows how far a blind trust in 'representations' might go.[81] He describes the attitude of medical pathologists involved in atlas making towards microphotography around the 1860s. Medical pathologists' interpretative work on diseases was based on microphotographs of specimens instead of the specimens themselves, with the photographic image perceived not as a mediator, but as the actual (real) micro world. Such attitudes, Breidbach argues, ended by discrediting the use of photography in science.

To end this introduction let me summarise its main points. Through an assessment of the different kinds of images contained in cell biology textbooks during the period 1950s-2000s, this study detects a visual change that manifests itself as images of a

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79 This refers to the lack of consideration of cellular approaches rather than the molecular for the understanding of life phenomena and for the possibilities of intervention for curing diseases.

80 Alberto Cambrosio, Daniel Jacobi, Peter Keating, Ehrlich's "Beautiful Pictures" and the controversial beginnings of immunological imagery', *Isis*, 1993, 84: 662-99.

81 Olaf Breidbach, Representation of the microcosm - The claim for objectivity in 19th century scientific microphotography, *Journal of the History of Biology*, 35:221-50, 2002.

molecular nature outnumbering those of a microscopical nature. This dissertation assesses a period from the molecularisation of biology (1970s-2000s) that has not been covered yet. Moreover, the focus is on images rather than epistemic content and on textbooks as main carriers of this visual discontinuity in cell biology. This study characterises the images involved in the visual change, microscopical and molecular by relating them to Peirce's signs and with this it argues for firstly, a move from an iconic towards a symbolic modality in cell biology and secondly, for an intrinsic and relational validity among images running through history to construct worthy knowledge, one that goes beyond the models and theoretical assumptions that they contain. The specific relation established in this study between the two main types of imageries (the microscopical and the molecular) to two different cultures of knowledge production inside the discipline, and in turn, to the two different types of scientific selves also constitutes an important contribution. By using Baudrillard's theory this dissertation aims to explain, what has been perceived recently by some researchers as 'the neglect of the cellular model', that is the use of models centred on cell-cell interaction rather than molecules to explain normal and pathological states of cells. Finally, by focusing on imagery and cultures of seeing this dissertation offers an alternative view on cell biology to that held by cell biologists. The intention is not to substitute theirs, but to produce an assessment that could bring a more comprehensive vision of the complex process of knowledge production through imagery in cell biology.

## Chapter 1. The imagery change in cell biology: What is it?

The imagery change that this study addresses refers to a gradual decline in the number of images obtained with microscopes, optical and electronic, and the concomitant rise in the number of images of a molecular nature in cell biology textbooks between the 1950s and the 2000s, a phenomenon that became more prominent from the early 1980's and is visually encapsulated by the transition from left to right shown in **Figure 1** (see page 20). I argue that this visual change represents, firstly, a sign change from iconic towards symbolic forms and secondly, the dominance of the molecular gaze and its methodological vision which is based on an hyper-mobility of signs.[82] The importance of this imagery change and hence one of the main issues that this dissertation argues for, resides in the fact that microscopical and molecular images not only belong to different epistemologies, but they differ substantially in the relation each of them have as representations to the referent (the object) they are supposed to represent; the cell.

The idea of a visual change in the discipline of cell biology is the direct result of my own experience, firstly as an undergraduate biology student (1980-1986), secondly as a PhD molecular biology student (1988-1991), thirdly as a researcher in cell biology (1992-2005), and finally, as a prospective PhD student on the history of cell biology (2005-to date). There are some crucial events that occurred during that period and beyond that despite their contingent character would shape my thoughts on the idea of a visual change. The way I see those past events today is like finding through time, cardboard pieces each with a distinctive form but lacking a picture and not knowing at the time that they were the pieces of a jigsaw. It is only now as I go along writing this dissertation that the pieces of the jigsaw are coming together and that a clear picture is emerging. The first event I recall was when I became an assistant lecturer during my 4$^{th}$ year (1985) as a master student in biology in Argentina for a course on 'molecular bio-mechanisms'. In organising the course a primary idea that arose was to look for images in textbooks that could trigger a quick visual impression on students on how cells do things, that is, how they synthesise proteins, secrete substances, divide, change shape and differentiate. In my search for sources, my first move was to select some cell biology textbooks and also to

82 Quantitative evidence for this visual change is provided later in this study (see charts 1& 2, qualitative analysis of textbooks, A.2 and tables, A.5 in Appendix).

keep an eye out for one or two on biochemistry. The existing possibilities for cell biology textbooks at the time were: *Cell biology* (CB) by De Robertis et al (1980), *The Cell* by Fawcett (1981) and *The Cell* by Brachet and Mirsky (1961).[83] It did not take me that long to realise that there were limitations to these sources. All in all, although excellent textbooks, they were either too 'cellular', that is, heavily based on microscopical images (De Robertis and especially Fawcett), or too technical and with only a few illustrations (Brachet and Mirsky). The choice for a biochemistry textbook had a similar outcome. In this case there were two prominent ones, the classic *Biochemistry* by Lehninger (1982) and that of Lubert Stryer (1981).[84] The problem with them was that although they were well written and profusely illustrated, they lacked a proper cellular contextualisation of the processes I wanted visually to highlight to students. Looking for alternatives, one day almost by chance I came across a textbook that at the time just arrived at the university library. That book was the Spanish edition of *Molecular Biology of the Cell* (MBC) by Alberts et al (1983). That finding was a breakpoint, for all the problems mentioned previously for the course, suddenly disappeared. MBC had in fact the virtue of visually (also textually) explaining all those cellular mechanisms that the others textbooks for one reason or another could not. What is more, even though MBC was printed in only three colours it was still a very didactical textbook to use for teaching. Some years later MBC became a constant companion during the writing of my PhD studies in Paris (1988-1991).

The second event that I recall acting as a primer for the idea of a visual change in cell biology occurred in 1994 shortly after I began my second postdoctoral appointment in the UK. I was at the library of the National Institute for Medical Research, in Mill Hill, London when I came across what as at the time the latest edition (3rd) of MBC (1994). The changes in this edition were significant. Not only that compared to its previous editions, MBC had more colours, but above all it had more images of molecules; one for almost every single cellular process you might imagine. This was also the time when I

83 Eduardo D P De Robertis, Eduardo M F De Robertis, *Cell and molecular biology*, Philadelphia, Lea & Febiger, 1980. Don W Fawcett, *The cell*, London Toronto WB Saunders Company Philadelphia, (1966 & 1981). Jean Brachet, Alfred E Mirsky, *The cell*, New York, New York Academic Press, (1959-1961).

84 Albert L Lehninger, *Principles of biochemistry*, New York. Worth, 1982. Lubert Stryer. *Biochemistry*, San Francisco. Freeeman, 1981.

began to work in the field of signal transduction in neurobiology.[85] The aim of the research was to describe the pattern of interacting proteins inside a neuron after its receptors interacted with those of neighbouring cells, a pattern that could provide a molecular explanation of the cellular process of neural migration during cortical development. The period that spanned the first (1983) and the third edition (1994) of MBC coincided with that of a sustained growth of the field of signal transduction, which alongside that of membrane associated receptors, are at the centre of the visual change I propose for the discipline. In effect, the 1990s was a period of sustained growth of this kind of imagery in scientific papers. The growth of this field was such that for many the overall picture was getting too complicated and at times quite confusing, especially in occasions when proteins suspected to have the opposing effect in a cellular process were found to interact with each other.[86]

My first years as a postdoctoral fellow in Britain were determinant in another sense. I became deeply interested in the history and philosophy of biology and in particular the social, cultural and political conditions of its development as a discipline.[87] The turning point was the reading of Thomas Kuhn's, *The structure of scientific revolutions*,[88] a book that my partner had offered to me four years earlier in November 1990 when I was a molecular biology student, but I could not read it at that time.[89] Highly motivated after reading Kuhn's *Structure* and other books and whilst still a

85 As anticipated in the introduction, signal transduction studies refer to those focusing on the intracellular events that occur inside a cell after an external substance interacts with a specific receptor in its membrane. Since its imagery is pivotal for the visual change its main characteristics will be explained later in this chapter.

86 In 1996, I had a publication rejected in *Neuron*, a well-known scientific journal because of this. I reported the interaction of the protein I was studying Focal adhesion kinase (FAK) with two others which were supposed to have antagonistic effects on the src signal transduction pathway. Despite having done the experiment four times and always getting the same result, the referees asked me if I was sure of what I was reporting. The paper was finally published in another journal: Norberto Serpente, Marie-Christine Birling, Jack Price, 'The regulation of the expression, phosphorylation and protein associations of pp125 FAK during rat brain development'. *Molecular and Cellular Neuroscience*, 1996, 7: 391-403.

87 Discussions with my former supervisor in Argentina Dr Emilio Levin were determinant for this.

88 Thomas S Kuhn . *The structure of scientific revolutions*, Chicago, London, The University of Chicago Press, 1970, (2nd edition).

89 I couldn't never fully read it because of my 'busy' times working in the laboratory doing experiments to finish my PhD in biology. I admit though having many glimpses at it during that period.

researcher, I completed first a bachelor degree in social sciences and later a masters in history and philosophy of science in a period of five years (1997- 2002). As a consequence of this my midfield (to use a football expression) incorporated more talents, among them Stuart Hall, Roland Barthes, Michel Foucault, David Harvey, Hans-Jörg Rheinberger, Jean Baudrillard, with many others staying on the bench. I ended not only having a good team, but also having a different set of spectacles to confront head on all the unanswered questions that my former profession left.

The last event I recognise as determinant for the idea of the visual change in cell biology arose when, many years later (2005) I was looking for a theme for a PhD dissertation in the history of science. I remember, in particular, one afternoon carpeting a spacious desk in the Wellcome library in London with all the editions of MBC (four editions at the time, in 2005) alongside some editions of other cell biology textbooks among them a couple of editions of CB from De Robertis (the first and the third editions, 1948 and 1965 respectively). The conclusions from such a preliminary visual survey could be summarised in the following statements. A) Present editions of cell biology textbooks display a vast variety of images, all different in kind **(Figure 2)**. B) In these editions images of a molecular nature, especially those describing molecules interacting to explain cellular phenomena (signal transduction, protein processing through cellular membranes and protein facilitated membrane transport) seemed to outnumber those produced by microscopes **(Figure 1 left and right respectively,** see page 20). C) A preliminary examination of textbooks from the late 1940s onwards suggests that this has not always been the case. Images of a microscopical nature were dominant from the 1940s until circa the late 1970s. D) Even though molecular imagery has always been present in cell biology textbooks this imagery showed different forms through the period assessed. Old editions for instance featured molecules on their own or as part of metabolic cycles, or from the 1960's until the late 1970s as part molecular mechanisms such as DNA replication and protein synthesis. During the period of the 1950s to the 1980s they represented a small number when compared to microscopical imagery with new expressions of this imagery emerging from the early 1980s.

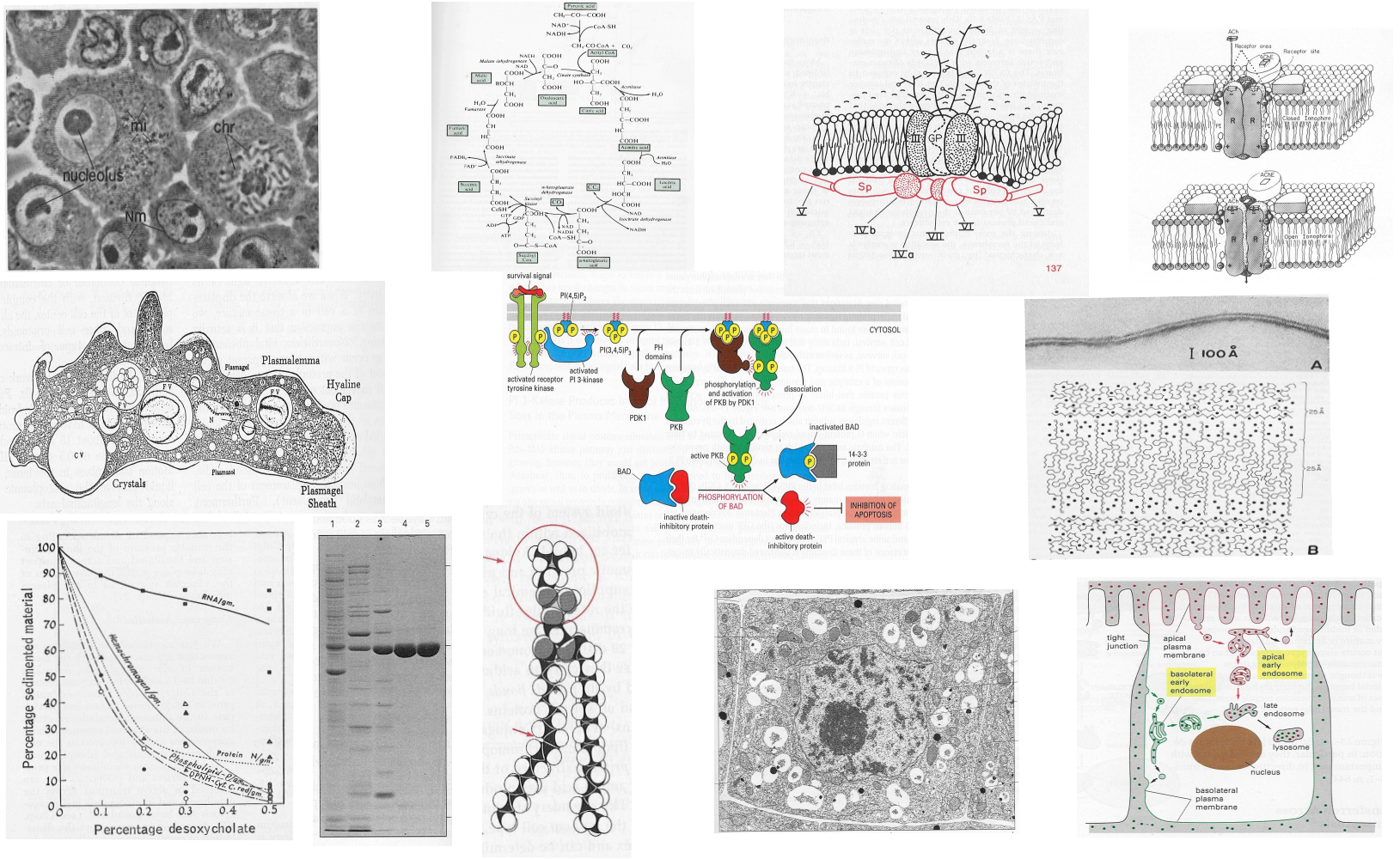


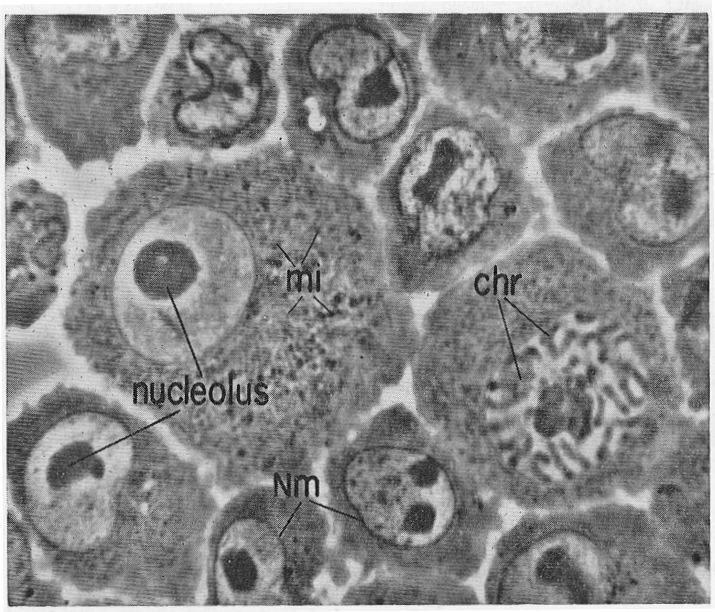

**Figure 2: The different types of images found in cell biology textbooks**

The next step for my PhD project was how to prove that there was some concrete phenomenon going on behind these preliminary observations. Many dilemmas and questions arose, chiefly among them: Since there were more textbooks on cells other than MBC and CB, which ones to look for? How do you compare one textbook from the 1950s with one from the 2000s when so many technological and epistemological changes have occurred between those years? Because of the vast variety of images present in textbooks, what would be the best criteria to classify them? Would it be possible to quantify the growth of molecular imagery in cell biology and if so, how exactly? Classifying images and selecting a source for this classification are two instrumental steps necessary to sustain the claim of a visual change in the discipline of cell biology. For organisational matters I begin with the issue of the classification of images and leave that of the selection of sources for the following chapter.

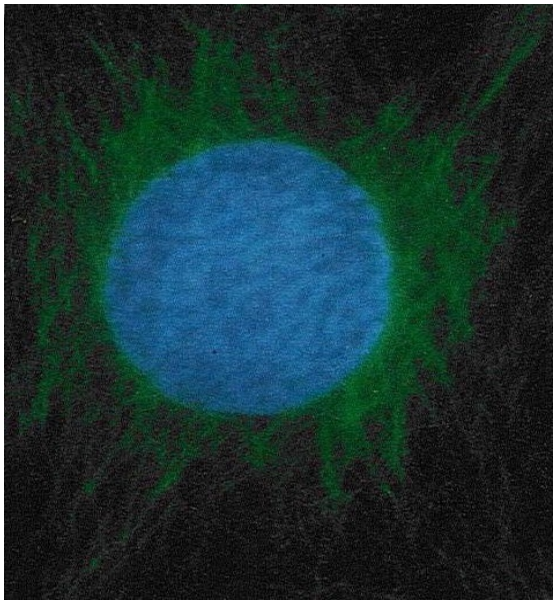
I propose to classify the different types of images displayed in present editions of cell biology textbooks **(Figure 2,** see page 51). according to their qualities and origins in the following categories.[90] 1) Optical images: Those obtained with different types of light microscopes and staining techniques **(Figure 3)**. 2) Images obtained with an electron microscope **(Figure 4).** 3) Images of drawings of cells or cell components, such as chromosomes, mitochondria, Golgi apparatus, ribosomes, etc not involved in any kind of cellular mechanism such as transport of vesicles during secretion **(Figure 5).** 4) Images of cellular models; those that visually describe the intracellular movements of vesicles and membrane fusion with small or no reference to specific molecules involved in those processes **(Figure 6).** 5) Images of models based on images taken with an electronic microscope ($e^-$ based models), **(Figure 7)**. These type of images, dubbed 'paired representations' by Michael Lynch, were widely used (and still are) in the heydays of electron microscopy (1950s-1970s), to attach a theoretical assumption to the image having thus as function to guide the viewer towards a particular interpretation of the electronic image.[91] 6) Images of molecular models of the third-generation **(Figure 8),**

90 These categories encompass the vast majority of images found in cell biology textbooks for the period surveyed. There are of course some images, which are of a hybrid character (containing an optical image and a drawing for instance) and hence difficult to classify.

91 Lynch, 1990, op. cit., pp. 153-86.




A



B

**Figure 3: Images of cells or cells components taken with an optical microscope**
**A) De Robertis et al, 1965.B) Alberts et al, 2002**

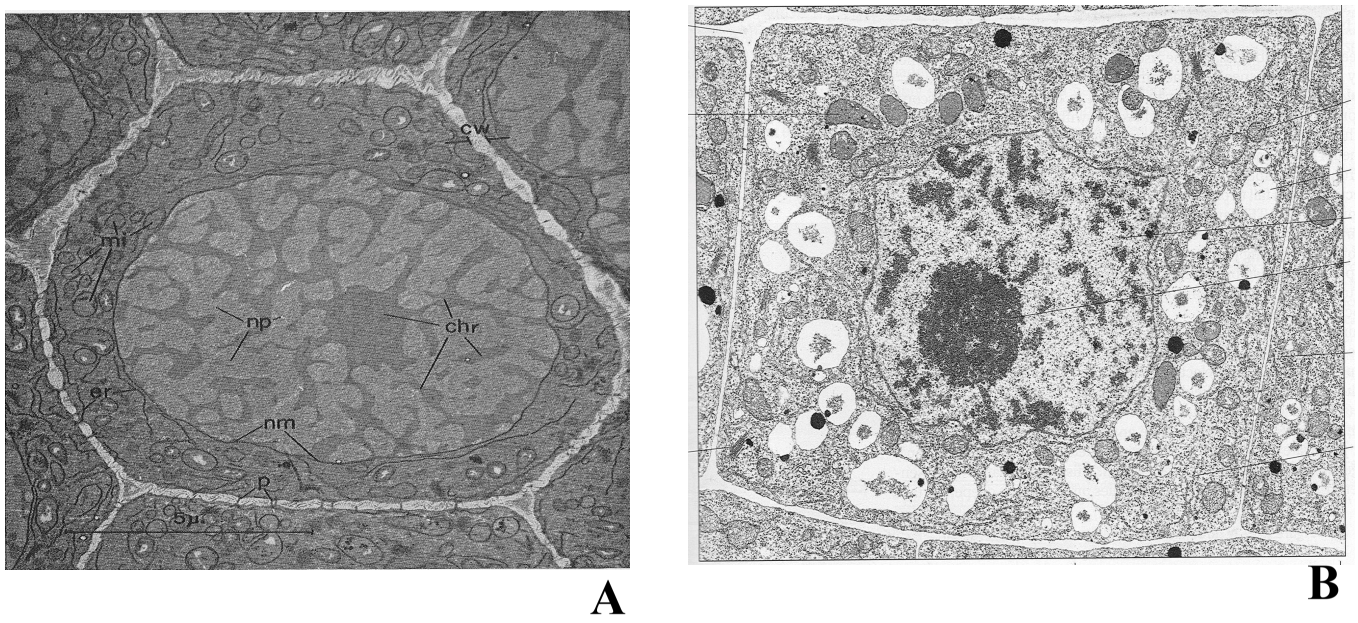
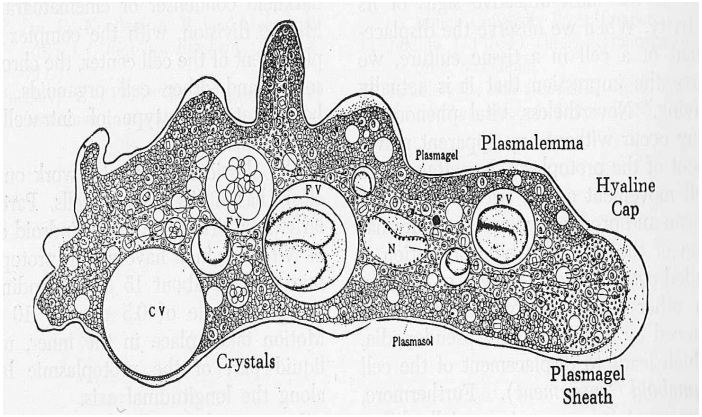
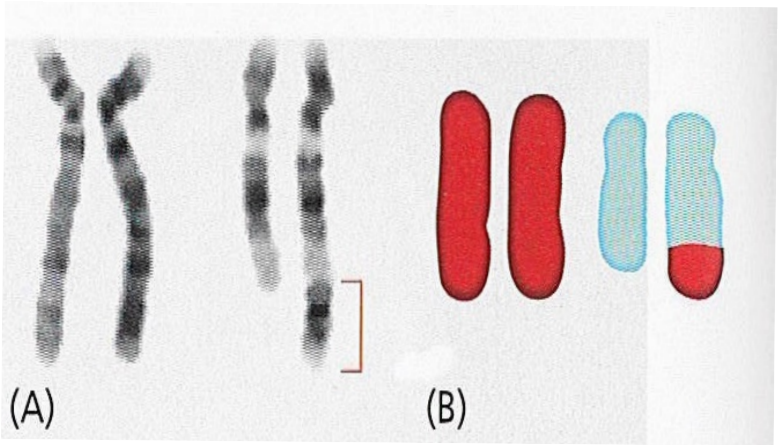



**Figure 4: Images of cells or cells components taken with an electronic microscope. A) De Robertis et al, 1965. B) Alberts et al, 1994**



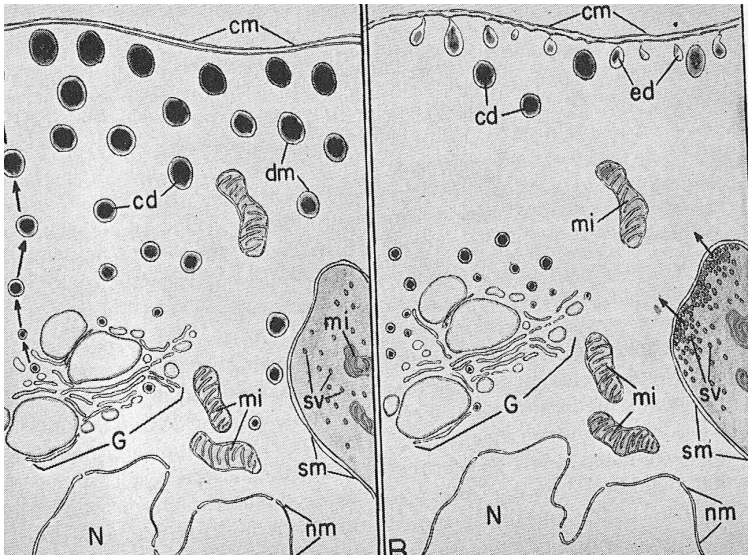

A



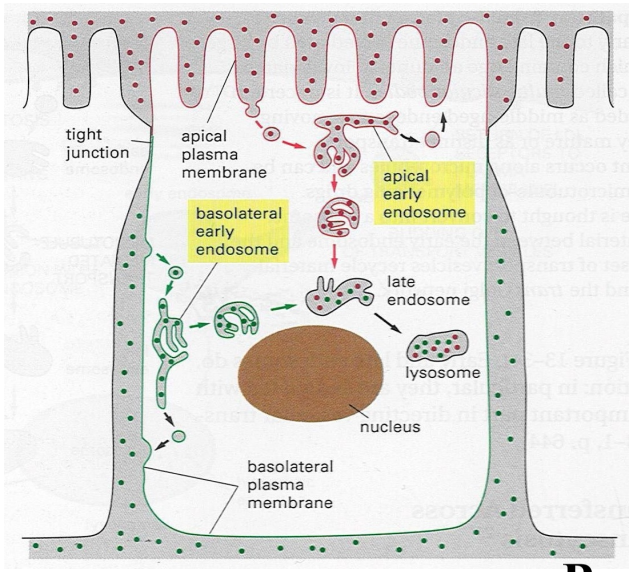

B

**Figure 5: Drawings of cells or cells components (isolated chromosomes, membranes, mitochondria. etc.)**

**A) De Robertis et al, 1965. B) Alberts et al, 2008**

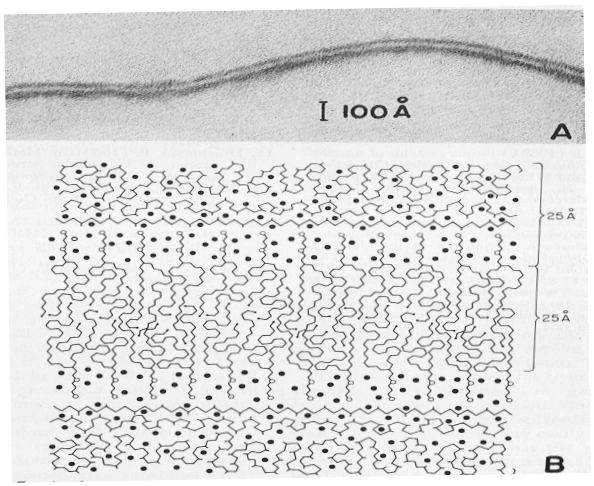



A

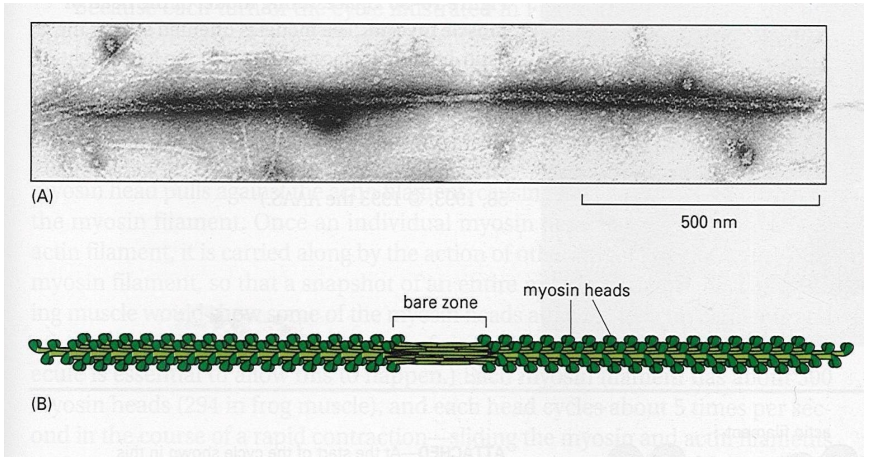



B

**Figure 6: Images of cellular models A) De Robertis et al, 1980. B) Alberts et al, 1994**

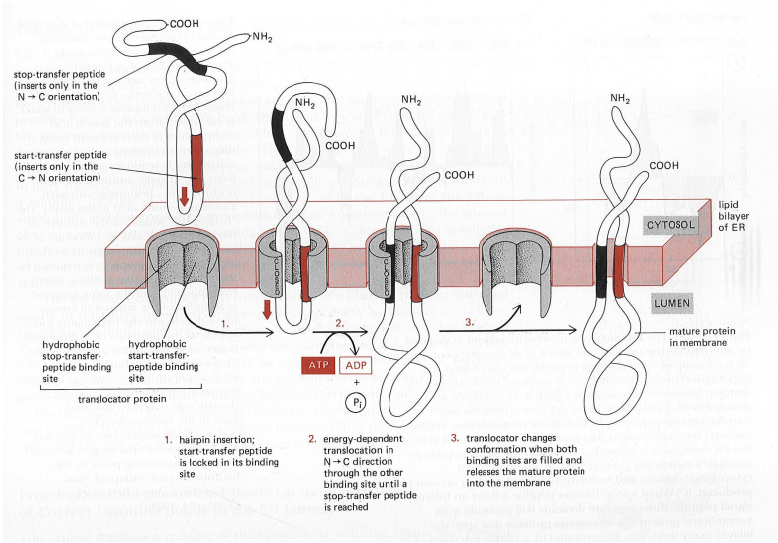


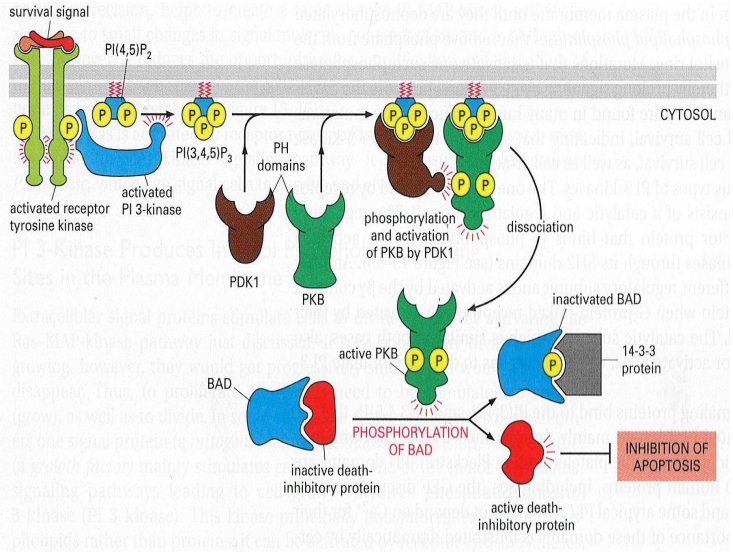

A




B

**Figure 7: Models based on images obtained with an electronic microscope.**
**($e^-$ based models: Paired representations) A) De Robertis et al, 1965. B) Alberts et al, 1994**




**A** **B**

**Figure 8: Molecular models belonging to the molecular culture (3rd generation models second order) A) Alberts, et al 1986 and B ) Alberts, et al 2002**

images that are conceptualised in this study as the latest form or expression of molecular imagery.[92] They include varied forms such as: a) models of protein synthesis and processing (maturation) as occurring in sub-cellular structures such as the endoplasmic reticulum, b) macromolecular transport by membrane associated proteins entailing a conformational change in them, and c) signal transduction and membrane embedded receptors with signalling functions. All of them are as their previous forms, created by imagination and convention through a process of translation. For the particular case of signal transduction, the main visual form involved in the visual change, the translation process includes the transformation of a visual output product from a combination of techniques of a biochemical and immunological origin (Immunoprecipitation/Western Blotting, 'IP/WB'), into visual ones.[93] 7) All other pictorial forms, such as diagrams, charts, pictures or drawings of instruments and or techniques, DNA or protein electrophoresis gels, autoradiograms, apparatuses, and the depiction of molecules on their own without any involvement in any type of cellular processes. **(Figure 9).**[94]

In what follows, a description is given of the main characteristics of the two images that this study focuses on: the microscopical and the molecular image **(Figure 1, left and right respectively,** see page 20), with some insights on their history, their connections with key epistemic events for the discipline and the conditions for their acceptance are discussed.

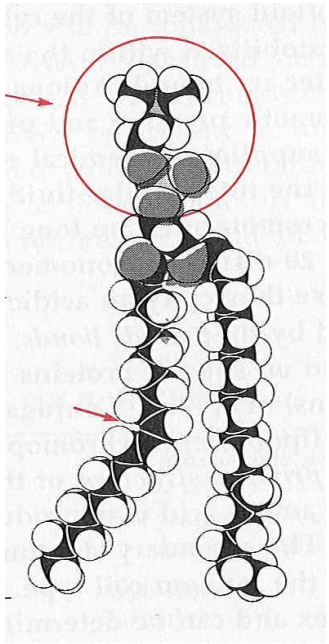
### 1.1 The microscopical image.

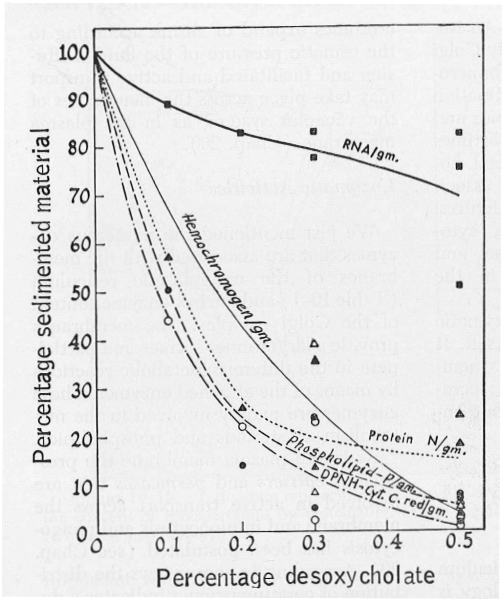
Microscopical images are at the centre of what the study of cells was and is about. That said, as we will see in this chapter the visual construction of the discipline of cell biology through the microscopical image had not always been characterised as a process of progressive epistemic continuity. Microscopical images are those that derive from

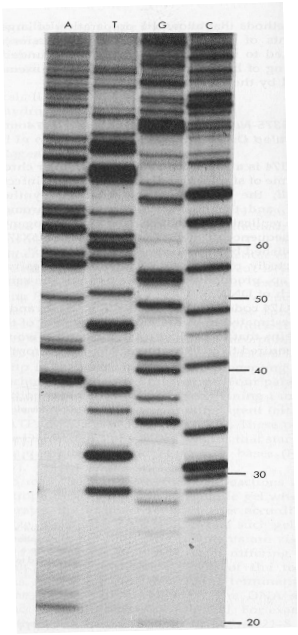
92 The historical development of the different forms of molecular imagery is explored later in this chapter.

93 See later the subsection on molecular imagery for more details on the process of transformation of imagery for this type of molecular models. Other techniques are currently used, apart from IPWB such as two hybrid system, and interactive proteomics, to study protein-protein interactions on cells.

94 These kind of images have shown little variance through the successive editions of MBC (data non plotted).






**A** **B** **C**

**Figure 9: All other pictorial forms: A) molecules (1st and 2nd generation models molecular culture, B) diagrams, charts. C) gels, apparatuses etc.**
**A) De Robertis et al, 1980. B) De Robertis et al, 1965. C) De Robertis et al, 1980**

magnifying devices such as optical and electron microscopes. These images are quite distinctive as are the operational physical conditions of the instruments that produce them. So, for instance, whereas the optical instrument uses light and glass lenses for the production of images, the electronic instrument uses electrons and magnetic lenses instead.[95] Both instruments however share some characteristics that set their images apart from those of a molecular nature. Firstly, the images that they produce result from the condensation (focus) in a visual plane of the scattered particles of energy that have passed initially through a chemically treated and stained specimen and subsequently through a magnifying lens. Secondly, optical and electronic images are based on the organising principle (metaphor) of extension of naked-eye vision (that they can achieve what the eye cannot) and that of a 'window into the invisible world'.[96] These two organising principles act in fact as two essential preconditions for the legitimacy of the imagery produced by both instruments.[97]

The first microscopic images date from the 1660s. They were produced by Antoni van Leeuwenhoek (1632-1723), who claimed for the first time to have seen *animalcules* (bacteria) with his single lens microscope, and almost simultaneously by Robert Hooke (1635-1703), who in his *Micrographia,*[98] coined the term 'cell' to refer to empty compartments when observing petrified and burnt pieces of wood (cork) with his double lens microscope.[99] These images of a minute, 'invisible world', were at the time, new extremely varied and above all without a consistent epistemology behind them other than

95 Other important differences are: the final place where the image of the specimen is projected and the preparation and state of the samples for observation.

96 After van Fraassen this metaphor together with that of 'mirror of nature' has been central for the philosophical thinking on science. See van Fraassen, 2008, op. cit., pp. 98.

97 Conceptualising images produced by an electron microscope as an extension of our eyes vision is a highly contested stance. See the Hacking/van Fraassen controversy in: Ian Hacking, 'Do we see through a microscope?', in P M Churchland C A Hooker (eds.), *Images of science: Essays on realism and empiricism,* Chicago, London, The University of Chicago Press, 1985 (The book includes van Fraassen answer to Hacking).

98 Robert Hooke, *Micrographia or some physiological descriptions of minute bodies*, New York, Dover Publications Inc, 1938, (originally published in 1665).

99 Hughes, 1959, op. cit. Harris, 1999, op. cit. See also John R Baker, The cell theory: a restatement, history and critique. Part I, *Quarterly Journal of Microscopical Sciences*, 1952, 93: 157-90.

just mere curiosity.[100] As such, they were far from belonging to a defined body of knowledge as are the ones we are accustomed exist nowadays. This situation of not having an episteme behind begin to change by the 1820s when microscopical images **(Figure 10)** began to become pivotal for the emergence and later establishment of cell theory; the proposal that cells are the minimal unit that expresses the essential features that characterises the living, over the inorganic matter, namely, metabolism and reproduction. In fact cell theory was the result of the many common features found in the images produced by optical microscopes of macerated vegetal and animal tissue that began to accumulate from the 1700s but with more focus and regularity from the 1820s.[101] Cell theory was originally proposed by Matthias Schleiden (1804-1881) and Theodor Schwann (1810-1882), but had important contributions from many other observers such as Rudolf Virchow (1821-1902), Robert Remak (1815-1865), and Jan Evangelista Purkinje (1787-1869) among many others.[102] After many disputes over its legitimacy, from around the 1920s onwards, cell theory, because of its ability to integrate all the diverse activities ascribed to the living realm, began to be increasingly accepted as a bedrock unifying assumption in biology and biomedicine.[103]

From the 1900s the microscopical image became important for the development of cytology as a discipline beyond its role for cell theory. Microscopical imagery (optical and electronic) is at the basis for instance of a very powerful image that has acted to visually convey the idea of the universality and centrality of cells for the study of biology. This refers to the image of the 'ideal cell type', a key pictorial construction of a cell built through the synthesis of many microscopical images serving to create the idea of a single integrated version of the cell **(Figure 11)**. This visual construction purporting to capture in a single snapshot the diverse morphological qualities of cells of different

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100 This lack of episteme behind the microscopical image would change with the establishment of the cell theory.

101 Hughes, 1959, op. cit., pp. 29-54.

102 Harris, 1999, op. cit.

103 The importance of unifying ideas for the history of biology has been highlighted by Vassiliki Smocovitis. He argues that the evolutionary synthesis (1930s-1940s) was one of those central unifying ideas for biology. Vassiliki B Smocovitis, *Unifying biology: The evolutionary synthesis and evolutionary biology*, Princeton, Princeton University Press, 1996.

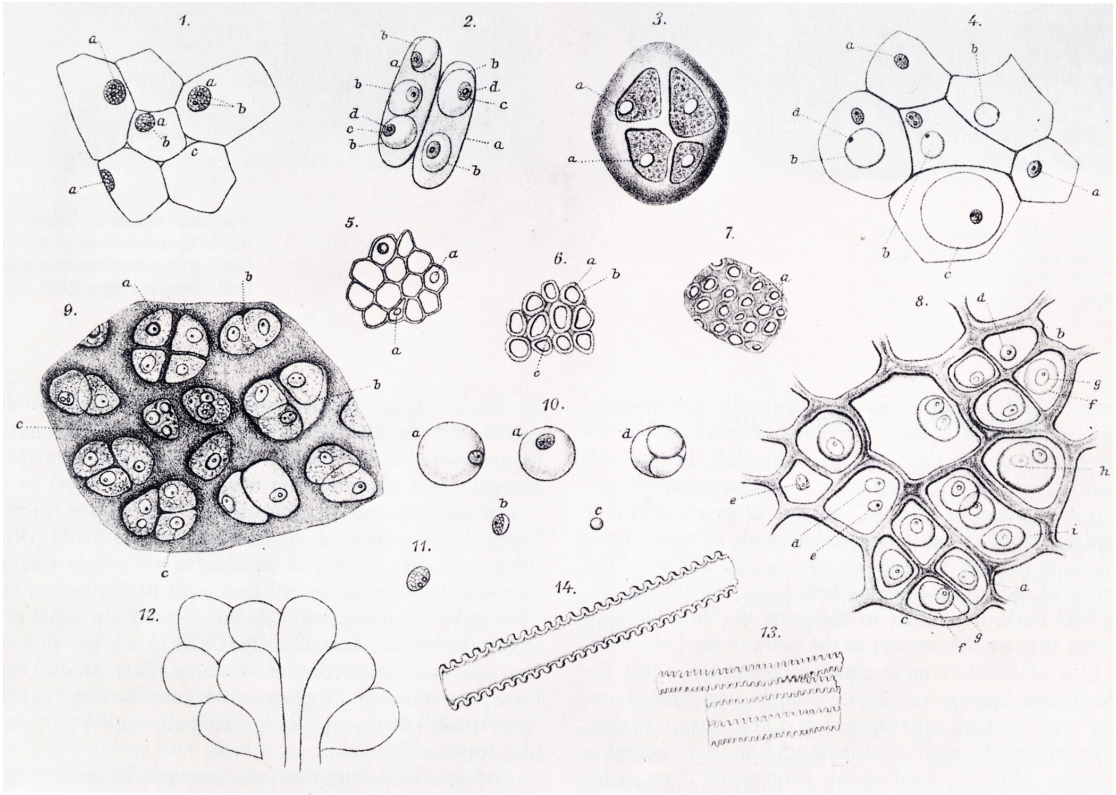
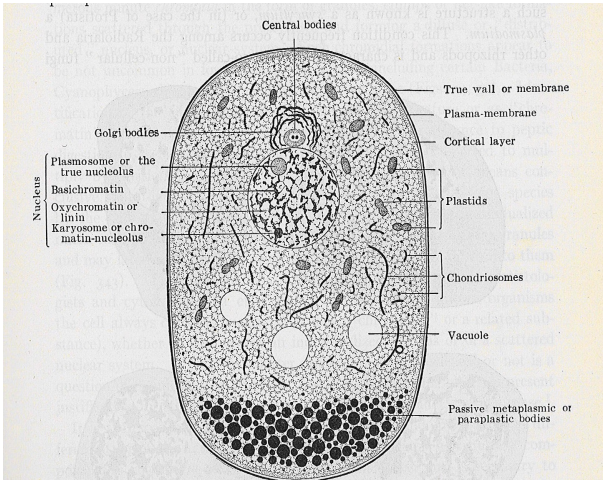
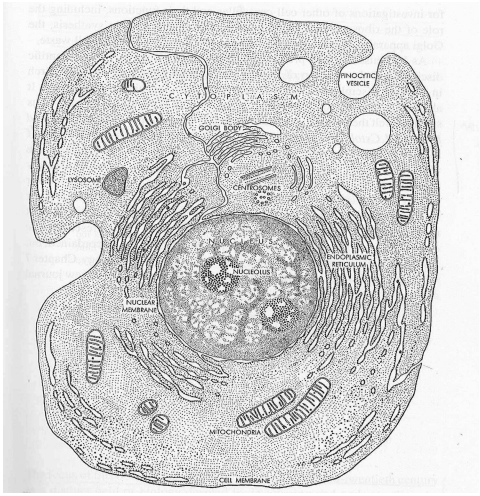


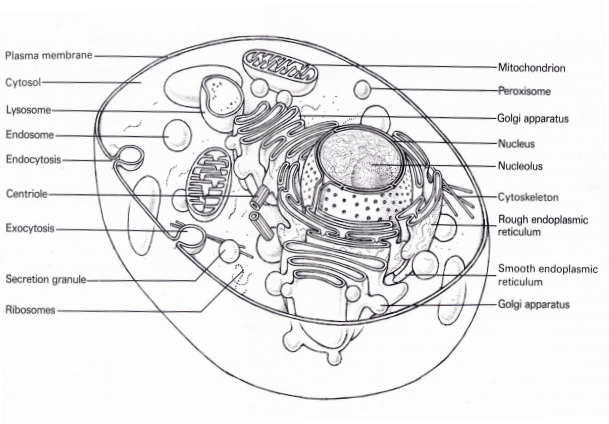
**Figure 10: Schwann drawings of different cell types, Schwann, 1839-1847**




A




B




C

**Figure 11: The Ideal Cell type. A) Wilson, 1925 B) Brachet, 1961, C) De Duve, 1984**

origins under various observational conditions would play an essential role on past and present unification of cell biology. Images of the 'ideal cell type' are present in the successive editions (1896, 1900, 1925) of one of the most prominent textbooks on cells, that of Edmund Beecher Wilson (1856-1939), are also present in most of the 1940s to 1960s cytology textbooks among them CB, and are still present in current editions of cell biology ones such as MBC.

### 1.1.1. The first limitations of the optical microscope imagery.

Optical images of cells were soon compartmentalised in two types, those that focused on the cell nucleus and those that focused on the cytoplasm. **(Figure 12)**.[104] This compartmentalisation was not just random. It was very much related to the differential topology and the associated functions that these two main parts of the cell manifested. More importantly, these two types of images went on to have different fates with regard to their perceived reliability as a means of defining 'the real' and consequently on their acceptability by early cytologists during a period that spanned from circa the 1900s to the 1930s. Wilson anticipated this differential view on the two cell components quite plainly; about the cytoplasm in the third edition (1925) he stated: 'The fundamental structure of protoplasm lies beyond the limits of microscopical vision and hence still remains a matter of inference and hypothesis'.[105] Years would pass by and this view will still stand true. Arthur F W Hughes (?-1975), an anatomist from the university of Cambridge who in 1959 wrote one of the first and most comprehensive works on the history of cytology remarked in it that until the late 1950s, 'it could be said of this branch of cytology' that considerably less has been achieved with certainty than in the study of the nucleus and its components'.[106]

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104 Research on the nucleus will expand towards cytogenetics and research on the content of cytoplasm on cytology; this last a discipline that would show a growing affinity towards physiological biochemistry. For more details on this see in this chapter subsection *'The role of electronic imagery in finding functions for structures: From cytology to cell biology (1940s-1960s)'*.

105 Wilson, 1925, op. cit., pp. 77.

106 Hughes, *op.cit.*, pp. 112, (by 'this branch of cytology' Hughes refers to the study of the cytoplasm).

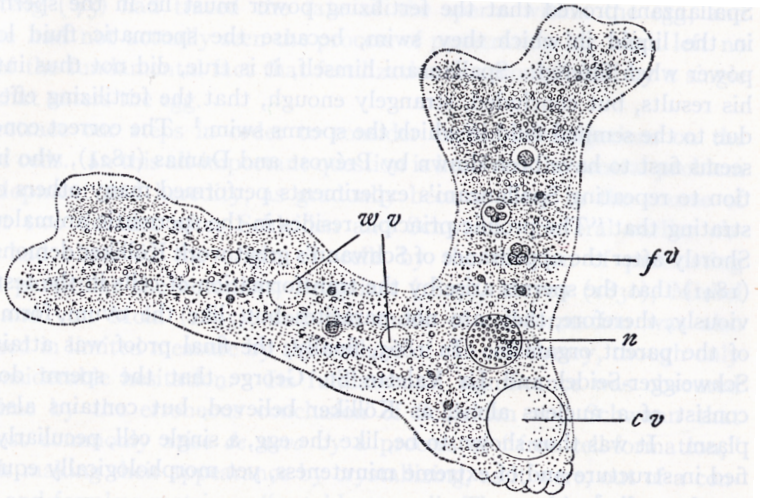


**Fig. 3.**—*Amœba Proteus*, an animal consisting of a single naked cell, × 280. (From Sedgwick and Wilson's Biology.)
*n*. The nucleus; *w*. *v*. Water-vacuoles; *c*. *v*. Contractile vacuole; *f*. *v*. Food-vacuole.

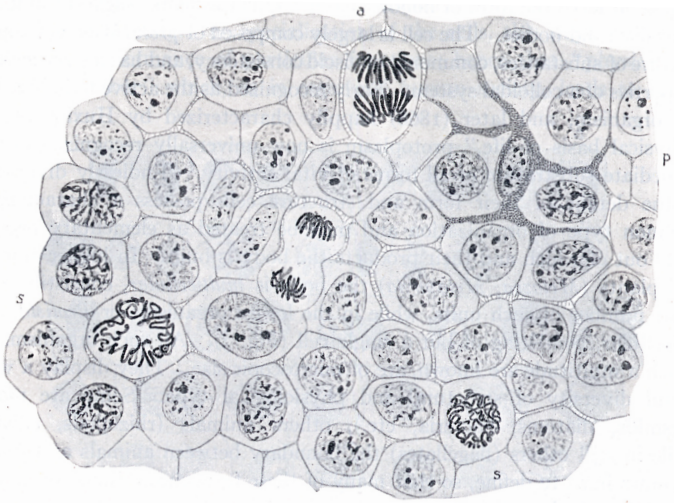


**Fig. 1.**—A small portion of the epidermis of a larval salamander (*Amblystoma*) seen in a slightly oblique tangential section, enlarged about 550 diameters. Most of the cells, polygonal in form, are in the so-called "resting" or vegetative (non-mitotic) state; but several are undergoing division (mitosis). Near *s* and *s* are spireme stages of mitosis, near *a* a middle anaphase, and near the center a late anaphase. Near *p* is a branching, granular pigment-cell that has crept up from below, forcing its way between the epidermal cells. Note the delicate plasma-bridges (plasmodesms) by which the latter are in many places connected. (This figure is combined from three separate camera drawings.)

**Figure 12: The contrasting imagery of the cytoplasm (left) and the cell nucleus (right) Wilson, 1925**

A key matter for the reliability and acceptance of images of the cell nucleus was the early cytologists' belief that they were observing 'material', 'tangible' structures. In effect, when compared to those of the cytoplasm **(Figure 13)**, images of the cell nucleus during cell-division revealed appealing images with larger, well-defined structures such as chromosomes and spindles[107] **(Figure 14)**. Nothing like that could be said however about the cytoplasm, which well until the 1930s remained 'visually elusive'. Despite being conceptualised as granular, fibrilar and reticular, its 'content' (particles) and especially its 'texture' (assumed molecular structure) were too small to produce credible images. In addition, no clear function, such as the one found for the nucleus, where chromosomes and cell division were associated, was found for them in the 1910s, except perhaps for the relation found between cytoplasmic sol-gel changes and cell movement. Even more problematic for the reliability of cytoplasmic imagery was the fact that obtaining images of cytoplasmic particles was a very unreliable process. The diverse observations depended on the different techniques employed for fixation and staining and often the same structure was given different names by different cytologists.[108] Many of the putative names given to the observed particles (plastidules, biophores, bioplasts, miscelae) represented only speculative attempts to materialise these structures as well as to make them meaningful.

Regarding the molecular 'texture' of the cytoplasm from the times of cell theory and well until the 1930s there were several theories accounting for its constitution. As anticipated above, the cytoplasm was described as granular, fibrilar, reticular, globular or even as structure-less and 'amorphous' by some observers.[109] A renewed hope for the optical microscope to deliver a reliable imagery of the assumed particulated content of

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107 This is why perhaps as Hughes notes with surprise (Hughes, 1959, op. cit., pp. 112), the use of the electron microscope was almost exclusively being directed to studies of the cytoplasm and not to the 'macromolecular structure of the nucleus and its components', because the expected level of visuality on the nucleus was considered tohave been achieved.

108 Issues of fixation and staining of samples alongside those of lenses aberration represented a serious problem for the credence on the microscopic image produced by optical microscopes.

109 Wilson and Nageli believed that the cytoplasm was conformed by'miscellae', a sort of 'imaginary particles that lied beyond the power of the microscope. Wilson speculated also with the notion of 'large molecular aggregates'. Cited in Ariane Droscher, 'Edmund B. Wilson's the cell and cell theory between 1896 and 1925'. *History & Philosophy of the Life Sci*ences, 2002, 24, 357-389, pp. 373.

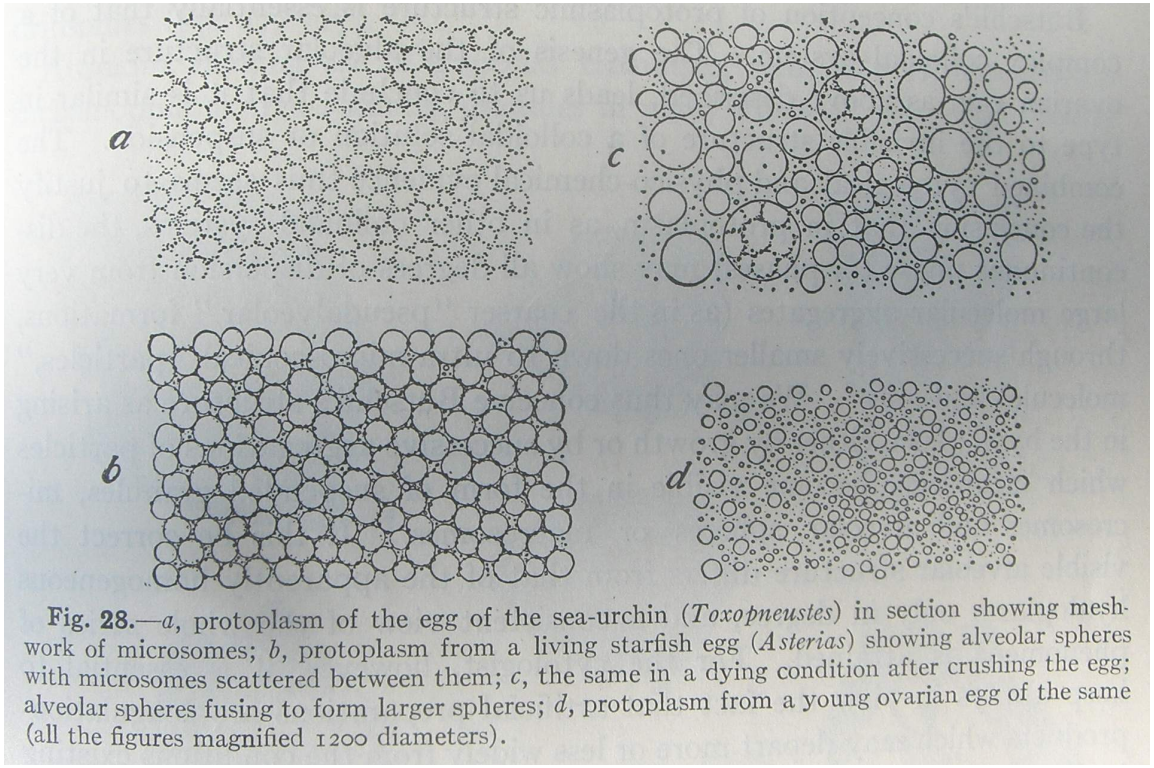


Fig. 28.—*a*, protoplasm of the egg of the sea-urchin (*Toxopneustes*) in section showing meshwork of microsomes; *b*, protoplasm from a living starfish egg (*Asterias*) showing alveolar spheres with microsomes scattered between them; *c*, the same in a dying condition after crushing the egg; alveolar spheres fusing to form larger spheres; *d*, protoplasm from a young ovarian egg of the same (all the figures magnified 1200 diameters).

**Figure 13: 1920s images of the cytoplasm. Wilson, 1925**

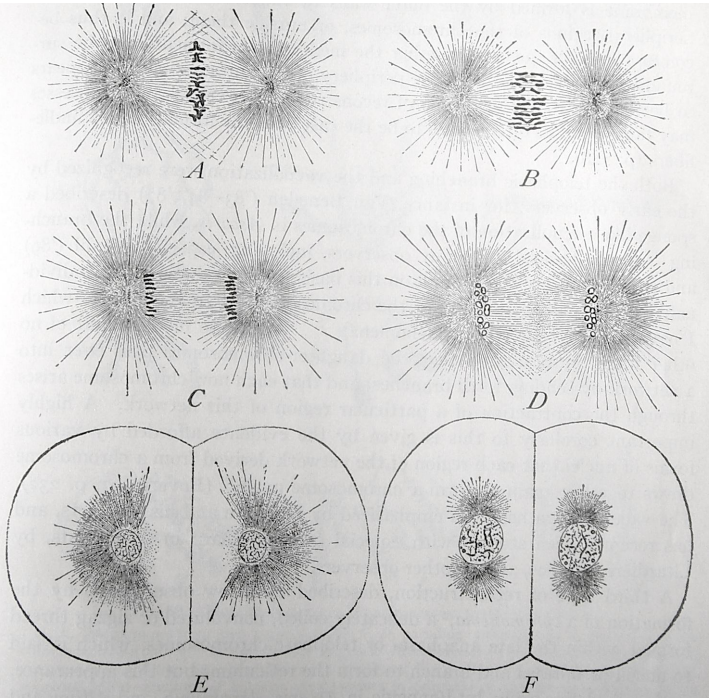


**Fig. 58.**—The later stages of mitosis in the egg of the sea-urchin, *Toxopneustes* (*A–D*, ×1000; *E–F*, ×500).

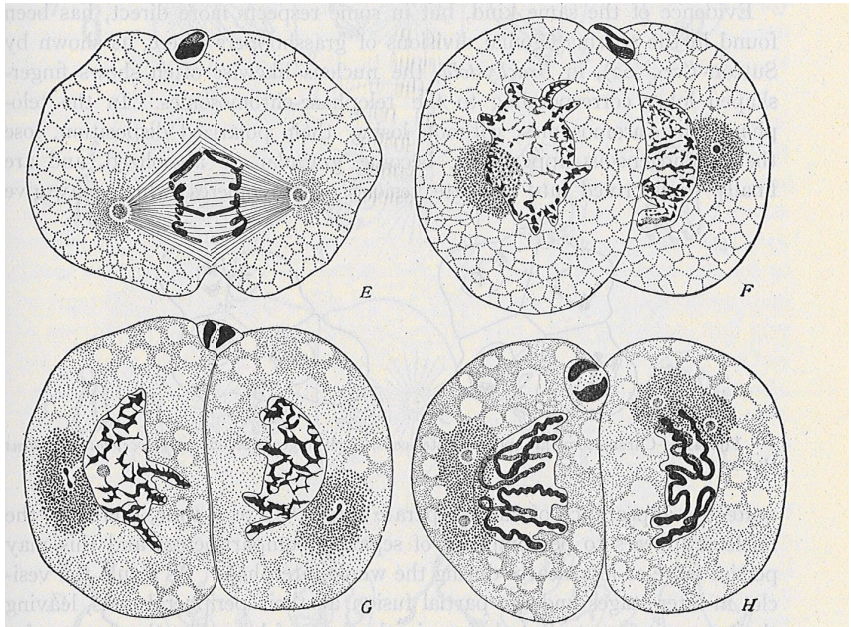


**Fig. 416.**—Individuality of the chromosomes in the eggs of *Ascaris* (BOVERI).

*E*, anaphase of the first cleavage; *F*, two-cell stage with lobed nuclei, the lobes formed by the ends of the chromosomes; *G*, early prophase of the ensuing division; chromosomes re-forming, centers dividing; *H*, later prophase, the chromosomes lying with their ends in the same position as before; centers divided.

**Figure 14: Images of cell division featuring the chromosomes and spindles. Wilson 1925**

the cytoplasm was boosted by the resolution of two of the main technical drawbacks the instrument had by the end of the 19th century, namely: the occurrence of poor contrast and the existence of chromatic aberrations. The first was solved by the development of a new generation of dyes and the second by the development by Ernst Abbe (1840-1905) in 1886 of apochromatic lenses.[110] This hope however did not last long, since controversy over the authenticity of its imagery in fact continued.

Abbe's optical theory did more than find a workable solution to correct lenses chromatic aberrations. It crudely exposed the limitations of the metaphor of the 'window into the invisible world', the kind of vision that allegedly the optical microscope offered. It was soon proposed that like our eyes, the instrument works inside a tiny little fraction (a band), of the spectrum of electromagnetic radiation corresponding to what physicists describe as the visible. The wavelength band of this region allows resolving, distinguish as separated, two points that stand at 0.2 microns of distance from each other, a longer distance than the one necessary to discern the internal structure of organelles such as mitochondria.[111] By the 1930s expectations ran high on the possibilities to develop new technologies that could extend the power of seeing by operating in another region of the energy spectra and thus being able to unveil the 'secrets' of the structure of the cytoplasm.[112]

110 Apochromatic lenses refers to a complex array of lenses arranged in a single unit used as objectives that make all the different colours of the spectra to focus in one single point reducing thus chromatic aberration. Chromatic aberration was one of the main suspects for the production of artifactual images in optical microscopy.

111 The capacity to distinguish two points that are close to each other as separate is known as the power of resolution of a viewing system. High magnifications are meaningless if they are not able to distinguish two near points as separate. The power of resolution depends on the energy of the spectra of electromagnetic radiation used. The optical microscope uses light and its radiation (550nm) allows for meaningful magnification of specimens in the order of 1000 times, with a power of resolution of 200 nm.

112 Other microscopes based on classical lenses like, phase contrast, polarising, ultraviolet and fluorescent were developed with the aim of improving on the power of resolution but none has achieved success in creating satisfactory images of the sub-cellular structure of the cytoplasm.

### 1.1.2. The expansion of microscopical imagery: The electron microscope.

The technological novelty promising to finally turn visible the sub-cellular structure of cells was the electron microscope.[113] The electron microscope was first developed in the 1930s in Germany with similar developments in other European countries such as France and Britain, alongside the USA and Canada.[114] The electron microscope differed from its optical counterpart because it uses electrons instead of photons.[115] Because of this the instrument has a bigger power of resolution being capable therefore to potentially distinguish structures, which are separated by 0.2 nanometres, and hence get 'meaningful' magnifications, which normally are thousands of times higher than those obtained with an optical instrument (the optical microscope resolve structures separated by 0.2 micrometers).[116] Although from the start its designers envisaged its application to the different branches of biomedicine, among them cytology, several difficulties prevented its use in this area. The main ones were, on the one hand, the incapacity of the beamed electrons to penetrate the thick specimens in use by cytologists at the time, and on the other, the instrument's incapacity to produce an acceptable level of contrast.[117] To overcome the first hurdle, the development of a sectioning apparatus, able to deliver ultra-thin sections of biological material was key. For the second, it was the search for substances that might act as the equivalent of dyes in optical microscopy.

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113 Rasmussen, 1997, op. cit. The electron microscope as Rasmussen has pointed out, was just one among the new and many expensive pieces of technology pushed by governments into research laboratories, as part of their wartime and post-war efforts to support basic research ('big science' projects); technologies that were willingly taken by scientists to advance their research agendas. In fact Rasmussen (1997, op. cit., pp. 8-9) considers that the history of the electron microscope was intimately related to that of molecular biology. Lily Kay sees it as a key instrument for the development of an instrumental and interventionist program on life. See Kay, 1996, op.cit., pp. 90. Electron microscopy was in fact considered as an allied technology to molecular biology, together with antibodies, electrophoresis, ultracentrifugation, etc, by important players in the development of the discipline like Sydney Brenner and Francis Crick. See: Judson, 1979, op. cit., pp. 207.

114 Rasmussen, 1997, op. cit., pp. 26. There are diverse types of electron microscopes, the one to be discussed here is called Transmission Electron Microscope (TEM) and is based on a beam of electrons directed to pass thorough a sample (specimen) after which an image is created in either a fluorescent screen (electron converted in light) or in a photographic emulsion (images as the ones showed in this study).

115 The power of resolution depends on the wavelength that is used. The electron microscope uses electrons, which have a shorter wavelength than the photons of the visible light and thus able to deliver a better power of resolution.

116 This is the equivalent to 500.000 times higher than the power of resolution of the human eye. By meaningful I mean a magnification that is able to resolve close points.

117 Rasmussen, 1997, op. cit., pp. 27.

Contrary to the development of the instrument, which was produced by large companies such as the Radio Corporation of America (RCA) in the USA and Siemens in Germany, the development of its associated technologies and techniques, like the sectioning apparatus, to improve sample preparation and specially the deployment of appropriate 'dyes' was to lie in the hands and dexterity of its users. Among the first and main users of the electron microscope who would play a key role in overcoming those technical hurdles and to produce a reliable imagery were: Albert Claude (1899-1983) a Belgian biologist, George Palade (1912-2008) a Romanian physician, Keith Porter (1912-1997) a Canadian biologist, Christian De Duve (1917- ), a Belgian medical doctor with a solid background in cytology and biochemistry and Eduardo Diego Patricio De Robertis (1913-1988), an Argentinean scientist and first author of CB.[118]

From the early 1940s and with more intensity during the 1950s and 1960s, a growing number of cytologists started to complement and even in many cases to replace the light microscope with their new chosen tool, the electron microscope and to work hard to adapt it to their research problems.[119] That said it is important to resist the impression that the assimilation of the electron microscope imagery in cytology labs was straightforward. Its use, even if, as mentioned earlier, it was based on the conception of visual continuity (with the optical instrument), it rested upon not only another type of physics (based on electrons rather than light), but also a somewhat different culture of observation, one that demanded a review of some of the existing conceptions of the nature of perception.[120] Besides, the imagery created by the electron microscope was

118 All the scientists mentioned contributed with several techniques to improve the use of the electron microscope. Claude, in 1947 designed the first prototype of an ultramicrotome from its predecessor the microtome Palade around 1952 developed a more efficient fixation technique using Osmium salt (heavy metals) in a specific pH media and the problems that would improve contrast. For more details see: Marcel Florkin, 'A history of biochemistry', in M Florkin and E H Stotz (eds), *Comprehensive Biochemistry*, Amsterdam, London, New York, Elsevier Publishing, 1972, 30, pp. 309.

119 Rasmussen 1997, op. cit. Rasmussen's book is in fact a rich account of the intricacies and polemics that sparked among the different users that went into from the late 1930s to the 1960s to transform it into a reliable image machine; contextualising it within the interests of governmental agencies and companies to promote its use.

120 Among them, to accept that an image created by deflected electrons in a fluorescent screen was the equivalent to one produced by a magnifier lens in a focal plane.

highly controversial and thus criticised on many fronts.[121] Among them, the impossibility to see electrons, and the damaging conditions of the electronic beam and sample preparation that were perceived as more damaging than those used with the optical microscope. The main issue at stake however, was that related to the interpretation of its imagery. Interpretative dilemmas would get even more convoluted for the case of cytoplasmic structures, which its images were on occasions of a 'fuzzy' nature **(Figure 15, A)**.[122] A good example of the issue of image interpretation is the one that took place in the 1950s over the internal structure of the mitochondria by Fritiof Sjostrand (1912-2011) and George Palade in the 1950s.[123] As this controversy suggests it was central for cytologists involved in the use of the electronic microscope not only to initiate a process of 'learning to see', but also to get quick consensus on what 'was to be seen'. The electron microscope produced images of entities that would later be shown to be 'real' like mitochondria, and some that would be finally be considered to be mere artefacts such as mesosomes.[124] In fact, it is not an exaggeration to affirm that achiving consensus on the determination of what counted as a genuine and reliable image and what was a fictitious one was the main trend in research laboratories in cytology and virology between the 1940s and 1950s.[125] It was only by the late 1950s after overcoming many technical and interpretative hurdles that a significant number of cytologists began to be reasonably confident about the reliability of the 'electronic image'. In Fleck's words the 'thought style' of the 'thought collective' of cytologists changed, as they developed a

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121 See for instance the Hacking/van Fraassen controversy in: Ian Hacking, 'Do we see through a microscope?', in P M Churchland C A Hooker (eds.), *Images of science: Essays on realism and empiricism,* Chicago, London, The University of Chicago Press, 1985 (it includes van Fraassen answer to Hacking). See also the many technical and conceptual issues raised in Hillman, et al. 1980, op. cit.

122 By current standards. See later on how the standardisation of electromicrographs become dependant on optical imagery **(Figure 15, B, inset,** see page 74**)**.

123 Bechtel, 2006, op. cit., pp. 192-209. Rasmussen, 1997, op. cit., pp. 124-152.

124 Nicolas Rasmussen, 'Facts, artifacts, and mesosomes: Practising epistemology with the electron microscope. *Studies in History and Philosophy of Science*., 1993, 24: 227-265.

125 Again, judged by the type of papers published in those times and by the discussions that followed every time a new sub-cellular structure was proposed to exist. For an extensive discussion on these issues see Rasmussen 1993, 1995, and 1997, pp. 124-49.

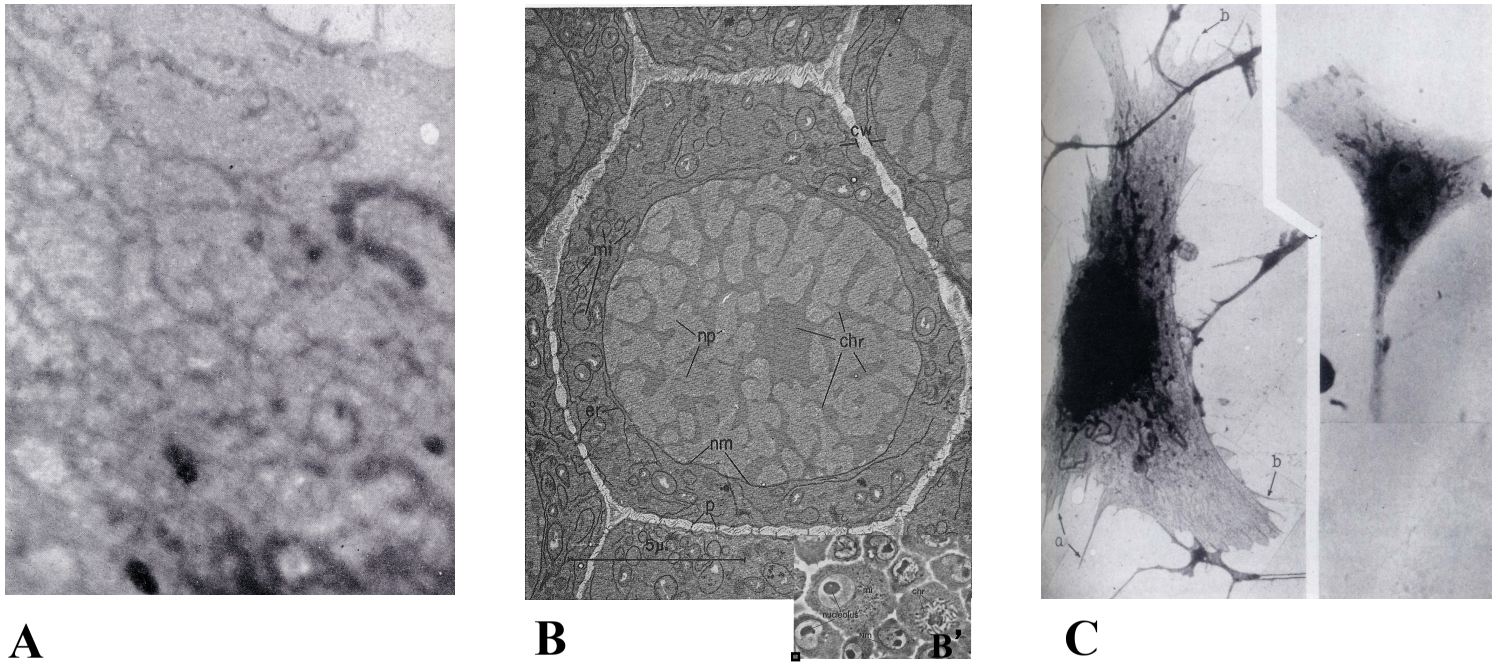



**Figure 15: Electron micrographs of cells. A) Porter, Claude and Fullam, 1945. B) De Robertis, 1965. B') De Robertis, 1965. C) Electron micrograph (left) and optical image (right) of a fibroblast, Porter, Claude and Fullam, 1945**

common experience on their ways of thinking during the process of training and specialisation to standardise the imagery of the instrument.[126]

Two phenomena played a pivotal role for the standardisation of the electron microscope imagery. Firstly, it was the establishment of a selection process for the vast panoply of emerging images (electron-micrographs). An opportune option was to select for display those images of cells that have visual elements close to the images obtained with the optical microscope **(Figure 15, B, inset,** see page 74). An option that proves correct Jacyna's assertion, when applying Hanson's conclusions on observation to his analysis of John Goodsir's own vision of cell theory in the 1860s, that 'new realms of experience are made intelligible, 'by assimilation to areas that are already ordered according to some conceptual and visual framework'.[127] Intelligibility, that seems to be independent of the time and technological device in use. Even more important for this process was the first composed picture of a fibroblast growing in a dish published in the *Journal of Experimental Medicine* in 1945 by Keith Porter and his collaborators. **(Figure 15, C,** see page 74**)**.[128] Despite criticisms about the artificiality of the cells growing in those conditions this image was one of the most convincing ones about the similarities of both kinds of observations, for literally two 'replica' samples of the same cells were taken to be visualised by both instruments.[129] Moreover, as a survey of the kind of images published in specialised cytology journals in the 1940s shows, a vast number of images were about the existence of sub-cellular structures previously observed with the light microscope. The second event key for the acceptance of the electron microscope imagery was the use of visual strategies that guided the viewer towards a particular interpretation. The deployment of 'paired representations', [130] a practice that emerged by the early 1950s and that endured in slightly different forms well up to the present, played that role

126 Fleck's concepts are discussed in more depth in Chapter 4 see subsection 4.3.2 '*Preferred viewing*'.

127 Jacyna, 1983, op. cit., pp. 80.

128 For the visual consequences that this image would have see Chapter 4 subsection 4.3: *'An alternative way to read the visual change: Reading images as signs'*.

129 Bechtel, 2006, op. cit., pp. 148. The importance of this eventuation of 'indexicality' is discussed in Chapter 4 subsection 4.3.3: *'Transfer of indexicality and iconicity into the images of a symbolic nature'*.

130 Lynch, 1990, op. cit., pp.153-86 and pp. 157-68.

**(Figure 7,** see page 57**)**. In a paired representation a drawing or diagram is placed alongside an electron micrograph with the aim of facilitating the process of interpretation of the raw image. As Lynch argues, the drawing might even take the form of a model when it adds theoretical information, which normally cannot be found on the photograph itself.[131]

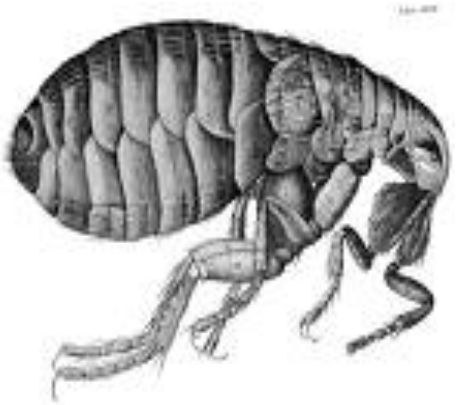
On a more speculative note, an important factor for the acceptance of the electron microscope images as reliable and truthful was that they were, framed under the continuity of vision argument[132] **(Figure 16).** This argument was originally used by early microscopists, such as Robert Hooke to render familiar to viewers small specimens by visually bridging microscopic images with those of naked-eye observations but only implicitly and without any epistemic justification **(Figure 16, A)**. This argument is still in use and proved essential for the justification of molecular imagery **(Figure 16, B)**. As such electron micrographs were considered to visually cover the 'middle ground' considered to exist between the optical images of cells by optical microscopes and the images of molecules given by another developing technology of the time (1950s-1960s) that of X-rays crystallography.[133] The X-diffraction pattern of collagen fibres for example, suggested a repetitive molecular structure for this protein, a phenomenon that coincided with similar regularity observed in electronic images of collagen.[134] Some cytologists, such as De Robertis, making intensive use of the instrument went even

131 Lynch argues that models 'reconstruct a holistic entity and seemingly return the viewer to a state of the object before it was analytically disassembled'. Lynch, Ibid. pp. 167.

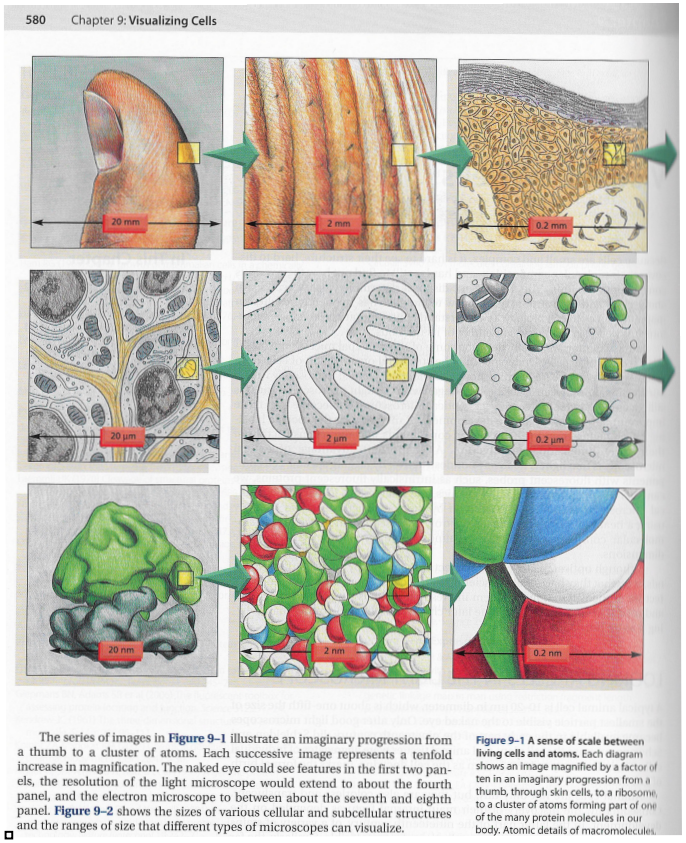
132 The 'continuity of vision' argument also known as the continuity of nature argument, holds that entities existing in the world are in a smooth continuum concerning their visibility and hence that there is no distinction to be made between the observable and the unobservable. It is based on the fact that there are overlapping areas of vision between, the naked eye and a magnifier, between a magnifier and an optical microscope, and between this last one and an electronic microscope and so on. In other words that there is an ontological continuity from what we see to what we cannot see. The philosopher Grover Maxwell, who first developed the argument as an argument for scientific realism, claimed that all entities are observable under suitable circumstances by using the proper instruments like a magnifier, an optical microscope, and so forth. Maxwell proposed it in times when electron microscopy was achieving a peak of acceptance. Maxwell, 1962, op. cit.

133 See later in this chapter the discussion on 3D models of proteins. Subsection 1.2.2. '*The second-generation models: The visual form of the second wave of the molecularisation inside cytology (1930s-1970s)*.

134 De Robertis, et al. 1948, Rasmussen 1997, op. cit. De Robertis, et al. 1975, op. cit., pp. 6.



A




B

**Figure 16: Visual versions of the continuity of vision argument through time.**
**A) Hooke, 1666. B) Alberts et al, 2008**

further and thought that the electron microscope could itself reveal the molecular texture of the cytoplasm.[135]

### 1.1.3. The role of electronic imagery in finding functions for structures: From cytology to cell biology (1940s-1960s).[136]

By the early 1940s the reigning climate for some cytologists was that visualising structure alone was becoming a meaningless endeavour and that consequently the science was facing a blind alley. Many cytologists, among them Eduardo Patricio De Robertis (the first author of CB) were committed to avoid that blind alley and began to follow instead a more meaningful path; that of investigating the biochemical processes those structures might harbour. For this, the attainment of direct evidence for some previous described phenomena seemed pivotal. That was the case of mitochondria for instance, which by the late 1940s its involvement in energy production derived only from indirect evidence.[137] Biochemists were also facing a similar blind alley to that faced by cytologists. Although, using the ultracentrifuge,[138] they found specific enzymatic reactions in the different ultracentrifuged fractions of sub-cellular extracts, they could not find where in the cell or in what particles those reactions were occurring. The solution envisaged by both groups was to produce images of those ultracentrifuged fractions with the help of the electron microscope. Electronic images soon began to reveal that the

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135 De Robertis, et al. 1948, pp. 63.

136 For more details on the transformation of cytology into cell biology see Bechtel, 1984, 1993, 2006. Florkin, 1972, op. cit., pp. 295-318. Joseph S Fruton, *A skeptical biochemist,* Harvard, Harvard University Press. 1992. Joseph S Fruton, *Protein enzymes, genes: The interplay of chemistry and biology,* New Haven and London Yale University Press, 1999.

137 Bechtel, 2006, op. cit., pp. 89. Observations correlated the presence of a particular sub-cellular organelle with the activity that a particular cell type was performing, like the increased number of mitochondria in active muscle cells for example.

138 The ultracentrifuge was another 'big science' technological device that developed during the post World War II period. (Rasmussen, 1997, op. cit.) Differential ultracentrifugation is a technique based on the use of the ultracentrifuge where cells are mechanically separated from tissues, then broken with the use of detergents and finally subjected to a series of centrifugations of increasing centrifugal force. The process entails several rounds of ultracentrifugation after which the different sub-cellular fractions are separated according to their mass and size (De Robertis, et al. 1987, pp 98-102).

ultracentrifuge fractions that accomplished a determined biochemical reaction such as the Kreb's cycle for instance, contained only mitochondria and no other structure.[139]

The merger that took place between biochemistry and anatomical cytology during the 1940s-1960s alongside studies on metabolic cycles, would represent an epistemic closure on a controversial subject that emerged in the previous century, that of the degree of dependency/independency of a biochemical reaction upon cellular structures. The first antecedent of this kind of studies is that of the 19th century studies on the fermentation of alcohols, the process by which yeast converts sugar into alcohol. Studies on alcohol fermentation by the end of the 19th century was divided in two camps regarding how the process occurred; both having enough empirical evidence to back up their claims. There were those who adopted Eduard Buchner's (1860-1917) ideas arguing that fermentation was just a chemical process that occurred independently of living organisms (structure) and those who adopted Louis Pasteur's (1822-1895) ideas arguing that alcoholic fermentation was a living matter (structure) dependent process.[140] Twentieth-century studies on aerobic cellular respiration started to focus increasingly on cells and thus to associate more intimately biochemical processes with cell structure.[141] Another event of particular relevance for the development of a visual imagery for biochemical processes and cell structure was the proposal by Otto Heinrich Warburg (1833-1970) that for enzymatic compounds to be functional they should operate in structured systems, systems that he imagined as 'membranes inside cells'.[142]

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139 See forthcoming subsection 1.2.2 on the imagery of metabolic cycles. *The second-generation models: The visual form of the second wave of the molecularisation inside cytology (1930s-1970s).*

140 William D McElroy*, Cellular physiology and biochemistry,* Prentice Hall Inc, 1961, pp 34-6. Joseph S Fruton, 'The emergence of biochemistry', *Science*, 1976, 192: 327-334.

141 That was the case research on intermediary metabolism, research that as I will discuss shortly concentrated more and more on individual cells as units of inquiry.

142 Bechtel, 2006, op. cit., pp. 108-109. During the 1930s and 1940s evidence mounted for processes like aerobic respiration occurring inside the internal membranes of mitochondria. Two main problems were at stake, firstly, the entire reaction of glycolysis, (the first steps in the conversion of glucose) could not be reproduced in a cell-free extract, secondly, oxidative phosphorylation could not be reproduced without the involvement of cellular membranes. Ibid. pp. 116.

The following extract from the cytologist Eduardo De Robertis in the preface of *General Cytology* (1948) succinctly summarises the state that cytology was in at the time.

> In its morphological aspect modern cytology has gone beyond simple description of structures visible to the light microscope, and by the application of new methods has begun analysis of the sub microscopic organisation which deals with the architectural arrangement of the molecules and micelles composing living matter. In its functional aspect, modern cytology has transcended the stage of pure description of physiological changes, and seeks an explanation of these changes in the intimate physicochemical and metabolic processes of protoplasm.[143]

What De Robertis' statement was also doing was to anticipate the final direction cytology took in the following years, that of relating a cellular structure to a biochemical, mechanistic (molecular) function.[144] It is unquestionable that this merger in the end entailed a total redrawing of the intellectual pursuits of cytology, which quite symbolically was renamed as 'cell biology'. This move was nonetheless far more than just a change of name. A new institutional identity arose for the study of cells, one that comprised new or renewed institutions to promote its aims such as the American Society for Cell Biology alongside new publications strategies and new journals such as *The Journal of Cell Biology*.[145] From the visual point of view, however, it is worth noticing that the visual form of metabolic cycles despite being assumed to occur inside cells were depicted in their own space without the involvement of cell structures **(Figure 17 A and B)**. Besides, electronic images of mitochondria were located in a different chapter to the image of the Krebs cycle.

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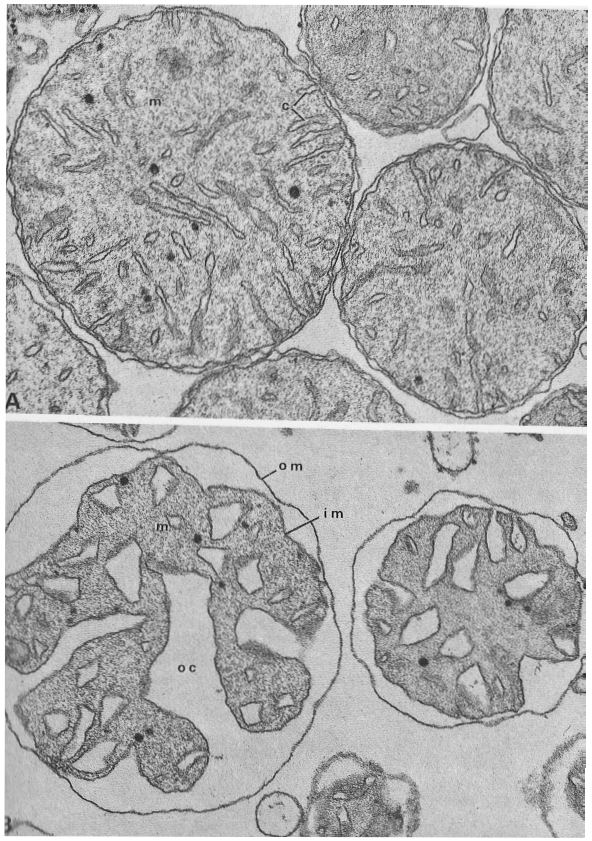
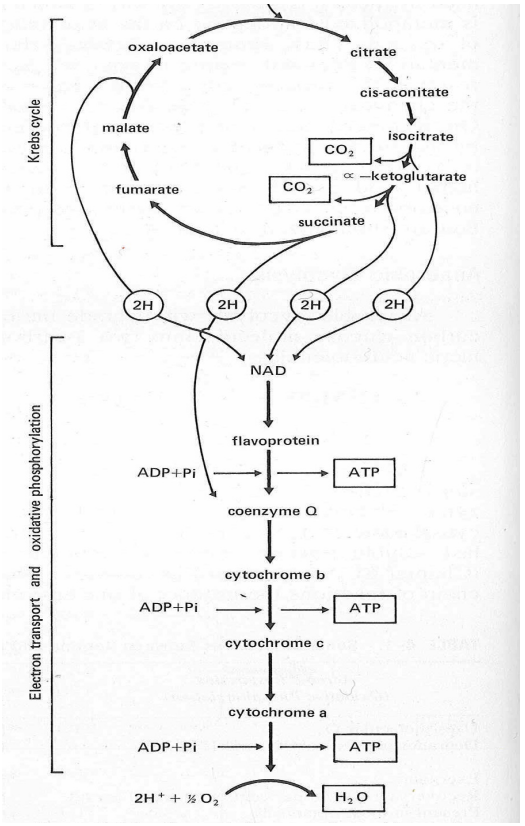
143 De Robertis, et al. 1948, op. cit., pp. iii.

144 Bechtel, 2006, op. cit.

145 Ibid. pp. 258-77. In my work I refer to this period as part of the second wave of molecularisation of cell biology (see the following subsection for a full discussion on this issue).




A




B

**Figure 17: Electron micrograph image of mitochondria and molecular image image of Krebs cycle and oxydative phosphorylation. A) Electron micrograph image of mitochondria. De Robertis. 1987. B) Image of Krebs cycle and oxydative phosphorylation De Robertis, 1975**

Most cell biologists as well many historians have hailed this period of merge between traditional cytology and biochemistry as an extra step of a process of constant and unidirectional expansion of knowledge on cells. This study however takes a different stance. It takes this process as rather an epistemic break.[146] The visualisation of sub-cellular structures and its association with biochemical functions entailed an association between morphology and mechanism in cytology that although it answered some of the old questions such as that of the dependency/independency of a biochemical reaction from cellular structures, created a new form of knowledge and above all a new discipline.[147] More importantly, it entailed the development of a new form of molecular imagery inside cytology.

## 1.2. The molecular imagery and cytology: An historical overview of its visual forms and its relationship with cytology (the three waves of molecularisation).

The microscopical image although the most obvious, is not the only one defining what cells are. The molecular image also plays a part in this process. Molecular imagery originates from a culture of knowledge that could be traced back to the 1790s with the work on animal respiration by Antoine Lavoisier (1743-1794), work that would be at the foundations of 18th century organic chemistry and 19th century biochemistry. Studies on respiration began focusing on whole animals as part of their studies on the conversion of heat during the physiological phenomenon of respiration and the identification of substances involved on it.[148] This focus would be transferred from whole animals first to

146 An epistemic break with a new associated imagery, but that it did not overlap with the microscopic imagery.

147 Whether viewing an old theme through the use of a new technology produces new knowledge or rather expands what is already known is a recurrent theme in the history of science. As Sicard notices, when analysing the use of photography for hysteric subjects by Jean Martin Charcot at the Salpetriere in 1870s, at least in some cases the use of a new technology, in this case photography did not secured new knowledge, but rather produced a new one. Monique Sicard, *La fabrique du regard: Images de science et appareils de vision (XVe- XXe Siecle),* Paris Editions Odile Jacobe. 1998, pp. 125.

148 William Coleman, *Biology in the nineteenth century: Problems of form and function*, Cambridge, New York, Port Chestern Melbourne, Sidney, Cambridge University Press, 1977, pp. 123-7.

tissues from circa the 1820s and later from around the 1910s onwards onto cells.[149] Paradoxically, this reductionistic transfer of focus would signify the emergence of a universal and global vision for the molecular sciences on life, that of explaining all biological functions at the molecular level. As a precondition for the development of that universal and global vision was the adoption and re-appropriation (from microscopical culture) of the idea of the extension of naked eye observations alongside that of a 'window into an otherwise invisible world' assisted by instruments and techniques. Although from a different nature the use of these ideas, proved in fact to be pivotal for the expansion of the molecular paradigm. These organising principles were/are so powerful, that makes, especially when used by molecular culture, almost disappear the role of 'instruments' from the practice of observation, as if observers were able to directly observe through their eyes without mediation. As we will see in what follows, whilst these organising principles have helped the construction a world of iconic images in the hands of microscopists, it has in the hands of molecular biologists served to create a different picture, one based on symbolic forms (see full discussion on the issue in Chapter 4). Some more differences between these cultures regarding their relation to the organising principles mentioned are also noticeable. Although molecular imagery also relies on the same principles as microscopical imagery, this reliance needs some extra justificatory steps, for they derive as we will see for the case of the latest form of visual in a complex process of translation of signs. In addition, as we will see in Chapter 5, to the eye-extension based imagery, molecular imagery has an extra organising principle, albeit of a wider nature, that of 'the network'.

Throughout the historical development of the molecular sciences several visual forms emerged **(Figure 18 A and B)**. The visual change described here is in fact the dominance over microscopical images of the latest of those forms (third-generation models). The differentiation of images into three types that this study proposes corresponds to three historical zones of epistemic convergence between the interests of molecular sciences in its different forms through history (organic chemistry,

149 This culture of knowledge is what I called molecular culture and its further characteristics will be discussed in Chapter 5.

**MOLECULAR CULTURE DEVELOPMENT IN ITS RELATION TO CELL BIOLOGY**

**VISUAL FORM**

**1st WAVE OF MOLECULARISATION (~1850-1930)** → **FIRST GENERATION MODELS**

* PAPER FORMULAE

**2nd WAVE OF MOLECULARISATION (~1930-1970)** → **SECOND GENERATION MODELS**

BIOCHEMICAL MODELS
* METABOLIC CYCLES (KREBS)

PHYSICOCHEMICAL MODELS
* 3D MODELS OF PROTEINS (COREY- PAULING)

MOLECULAR BIOLOGY MODELS
* DNA DOUBLE HELIX (WATSON/CRICK)
* DNA REPLICATION (MESELSON/STAHL)
* PROTEIN SYNTHESIS (CRICK/ORGEL)
* OPERON (JACOB/MONOD)

**3rd WAVE OF MOLECULARISATION (~1970-2000)** → **THIRD GENERATION MODELS**

* SIGNAL TRANSDUCTION/ INTERACTOMICS
* MEMBRANE EMBEDEED RECEPTORS WITH SIGNALLING FUNCTIONS
* ENDOPLASMIC RETICULUM PROTEIN SYNTHESIS AND PROCESSING

**Figure 18 A: The historical relation between molecular culture and cell biology (left) and its correspondent visual forms (right)**

**Figure 18 B: The different visual forms of molecular imagery:**
**a) Paper Formula (1st generation). b) Metabolic cycles (2nd generation). c) 3D models of proteins (2nd generation). d) DNA replication (2nd generation). e) Signal Transduction (3rd generation).**

biochemistry, molecular biology) and those of cell biology **Figure 18, A left,** see page 84**)**.[150]

Based on the concepts of 'molecularisation' and that of 'the molecular vision of life', these zones of convergence could be viewed as waves or entries of molecular sciences, inside cytology.[151] The first wave runs from the 1850s to the 1930s, the second from the 1930s to the 1970s and the third, from the 1970s to the 2000s **(Figure 18 A, left,** see page 84**)**.[152] To each wave of molecularisation **(Figure 18 A, left,** see page 84**)** corresponds a particular visual form or kind of imagery, imagery that is, basically based on models **(Figure 18 A, right,** see page 84). So, to the first wave correspond images of the first-generation models, which are basically models of molecules themselves depicted on paper, known as 'paper formulae' **(Figure 18 B, a,** see page 85). To the second wave, correspond images of the second-generation models, which are varied and of different nature (origins). Among them: biochemical models (metabolic cycles) using paper formulae, physicochemical models (3D models of proteins), and models from molecular biology from circa the 1950s to the 1970s (double helix, DNA replication, operon, protein synthesis, etc) **(Figure 18 B, b, c and d,** see page 85**)**. Finally to the third wave of molecularisation in cytology correspond images of the third-generation of models. These images include models of protein maturation through sub-cellular membranes (endoplasmic reticulum and Golgi apparatus), membrane transport by trans-membrane protein complexes (channels) and more importantly images of signal transduction and membrane embedded receptors with signalling functions **(Figure 18 B, e,** see page 85**)**. These three waves of molecularisation and their associated imageries respectively

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150 A periodisation was proposed for the 'progressive colonisation' of biology by molecular culture. See: Pnina G Abir-Am, 'The molecular transformation of twentieth-century biology', in J Kriege and D Pestre (eds), *Companion to science in the twentieth century*, London, New York, Routledge, 2003, pp 495-524. This periodisation does not contemplate the analysis of visual forms.

151 Molecularisation refers to the conceptualisation of all functions attributed to life as produced by an internal network of interacting molecules. Molecularisation connects with other related terms such as 'the molecular vision of life', (see Kay,1993, op. cit) and with the concept of 'molecularising' as defined de Chadarevian, et al. 1998, op. cit. (See introduction for more details).

152 This is possible if, as 'the molecular vision of life' thesis claims, molecularisation is taken as phenomena of epistemic colonisation of other disciplines. Of course this proposed periodisation is not absolute, so a new period with its respective practices and imagery did not mean the extinction of previous ones.

connect with the following three key epistemic events for the history of cell biology respectively namely: a) the paradigmatic change from colloidal to corpuscular chemistry (1900s-1930s), b) the merger of biochemical and cellular explanation and the sub-cellular localisation of metabolic cycles (1940s-1960s), alongside the appearance of the first 3D models from molecular biology (1950s-1970s), and c) the need of molecular biology to test the universal validity of the molecular mechanisms described in bacteria and viruses in higher organisms, by the use of, at the time, new technes such as that of genetic engineering and other biochemical and immunological developments (1970s-2000s).

### 1.2.1. The first-generation models: The visual form of the first wave of the molecularisation inside cytology (1850s-1930s).

Molecular imagery had a degree of development independent of knowledge of cells, before it began to become, from the 1930s, increasingly integrated with it. The first images displayed by organic and physiological chemistry and later biochemistry were just paper formula; what I have dubbed first-generation models **(Figure 18, A and Figure 18 B, a,** see page 84 and 85 respectively**)**. First-generation models or paper formula are two Dimensional (2D) depictions of molecules of an organic origin. They are symbolic forms where the letter stands for the atoms that conform the molecule (C is carbon for instance) and the line connecting the atoms stand for the interaction that keeps them together (covalent link). Introduced by Jacob Berzelius (1779-1848) in 1813, paper formulas evolved into several forms throughout history. All varieties are characterised by one common element. They bear a close relationship with the practices and experimental needs of chemists when synthesising and/or purifying different substances in their labs, that of naming and describing them in a sort of symbolic lexicon.[153] There are several forms, but the one showed in **Figure 18 B, a,** (see page 85), known as the structural form, which derives from the ones first created by the chemist Friedrich August Kekule (1829-1896) is one of the most representative. The aim of structural formulas is to describe the type of bonds between atoms in a molecule. This sort of molecular anatomy is based on the covalent bond theory (the sharing of electrons between atoms to account

153 Klein, 2001, op. cit.

for that bond). Later, after the discovery of isomerism in 1827, paper formula began to also give information of the type of spatial arrangement of those atoms in a 2D form on paper. Hermann Emil Fisher (1852-1919) and Walter Haworth (1883-1950) developed projections to visually express these differences for monosacharides; projections that would be extended later to other organic products like aminoacids. Images of this visual form are still part of the imagery content of textbooks in cell biology. The function of images containing paper formula in early cytological treatises as well as in current ones was/is to symbolise the molecular difference among the different substances that conform the cell.

### 1.2.2. The second-generation models: The visual form of the second wave of the molecularisation inside cytology (1930s-1970s).

The first of these three visual forms is that of intermediary metabolism, the biochemical cycles of reactions alleged to occur inside the sub-cellular structures involved in the latest steps in the degradation of sugars to produce energy (metabolism). **(Figure 18 B, b,** see page 85**)**. Because this imagery carries more information than that of a molecule in itself, I categorise it as belonging to the second-generation models of the second wave of molecularisation. Images of metabolic cycles describe in a circular and sequential pathway the chemical reactions in which products transform into another under the action of specific enzymes releasing energy. In these depictions arrows are used to connect the transformed substances (expressed as paper formula) that are part of a cycle, creating an interactive space similar to the one research on cybernetics was creating at the time.[154] Other symbolic depictions, including words, such as pyruvic acid, instead of chemical formulas to name substances emerged with time and were used also as an alternative for the construction of cycles. An important point to notice from these images is how they visually convey an idea of permanency despite of this being a very dynamic process. One of the most emblematic images of this type of visual form of the second-generation models is the one known as the Krebs cycle (also known as the citric

154 Cybernetics was an emerging field in the 1940s that originally tried to understand communication processes in machines and organisations and that soon expanded to life forms. It was first developed by Norbert Wiener (1894-1964) and included the key concept of feedback loops, a concept that was quickly adopted in intermediary metabolism studies.

acid cycle and the tricarboxylic acid cycle), **(Figure 18 B, b,** see page 85**)**.[155] During the 1950s and 1970s this visual form swiftly expanded inside biochemistry and also cell biology textbooks by incorporating other process other than the metabolism of glucose such as for instance the synthesis and degradation of proteins, nucleotides and lipids.[156] Despite the growth of images of intermediary metabolism and the increased presence of biochemistry and hence its imagery inside cytology, microscopical images continued to dominate the field during that period. Moreover, as anticipated earlier both types of images were to remain noticeably separated. **(Figure 17,** see page 81**)**.[157]

As mentioned before images of metabolic cycles such as that of Krebs, proved to be crucial for the view that the cell protoplasm was not a structureless 'sack full of enzymes' (a view supported by many biochemists before the 1940's) and was instead a highly structured system where biochemical reactions took place.[158] Another independent development pushing forward the idea of a highly structured cytoplasm was the change from the colloidal to the macromolecular paradigm in chemistry, a change that when associated with other developments ended by producing a new visual form, that of three dimensional (3 D) models of proteins.[159] **(Figure 18 B, c,** see page 85**).** 3 D models of molecules, the second form of second-generation models**,** began to emerge by the mid 1930s partly as a consequence of epistemic changes that began to unfold about 20 years before.[160] As we saw earlier, one of the problems that puzzled early cytologists

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155 The Krebs cycle is a series of cyclical chemical reactions occuring inside the mitochondia of cells which involves the chemical conversion of food molecules such as, sugars, lipids and proteins to produce energy (Alberts, et al. 1983, op. cit., pp. 72-3.).

156 Intermediary metabolism is sometimes equated to pathway biochemistry. This kind of research would dictate the agenda of biochemistry to almost the late 1970s.

157 The images of mitochondria are in chapter 12 'Mitochondria and oxidative phosphorylation' pp 273, and the images of the cycles are in Chapter 6 'Enzymes bioenergetics and cell respiration'. De Robertis, et al. 1980, op. cit., pp. 111.

158 Fruton , 1992, op. cit., pp. 105-107.

159 The 3D molecular models I refer to here are those developed in the 1940s by Linus Pauling (see later). They have a precedent in the models developed by Kekule in the 1860s, see Christoph Meinel 'Molecules and croquet balls', Chapter 9, in *Models: The third dimension of science*, S de Chadarevian Soraya, N Hopwood (eds.) Stanford, California, Stanford University Press, 2004, pp. 242-75.

160 An important contribution has been recently made on the subject of models in three dimensions: de Chadarevian, et al. 2004, op. cit. The 3D models analysed run from wax models of organs for research in

epistemologically and visually was that of the 'texture' of the cytoplasm.[161] Although early cytologists, like Wilson, suspected that molecules were part of that medium (texture) of the cytoplasm, they had no idea of 'what they looked like'. The first theory that claimed to understand the state of matter of biological origin was colloidal theory. Colloidal theory dominated the scene during the first two decades of the 20th century concerning the explanation of the structural medium of the cytoplasm (its 'texture').[162] Nevertheless, colloidal theory lacked an imagery of its own. Despite lacking a defined imagery there were speculations about small molecules arranging themselves in different conformations to produce the different states proposed to exist for the cytoplasm, to explain movement for instance (sol/gel and/or fibrilar/foam like transformations).

Osmotic studies, measuring the pressure of purified proteins on membranes in the hands of Soren Sörensen (1868-1939), soon began to show that molecules produced much larger pressures than those proposed by colloidal theorists thus leaving the door open for alternative theories.[163] A serious contender to colloidal theory was 'macromolecular theory', which was originally formulated by Hermann Staundinger (1881-1965) around 1926.[164] Macromolecular theory proposed that substances like proteins rather than being aggregates of small units, were single high mass molecules formed by certainly far more than forty atoms through strong covalent bonds. If the structure of proteins was to be colloidal that meant that its molecular mass was to be as that of the average mass of the different aggregates. If it was to be macromolecular instead, it had to have a well-defined and much bigger value. In 1926, Theodor Svedberg

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human anatomy in the 19th century to 3D models of molecules in 19th century chemistry and 20th century molecular biology all serving quite varied purposes.

161 Ultrastructure meant two things to cytologists: 'particles' such as the Golgi apparatus, mitochondria, chloroplasts, etc, and also the molecular medium (texture) in which those structures were embedded and the substances those structures were made of.

162 Robert Olby, *The path to the double helix*, Seattle, University of Washington Press, 1974, pp. 3-21. Florkin, 1972, op. cit., pp. 279-294. Fruton, 1999, op. cit., pp. 196-207.

163 Fruton, 1999, op. cit., pp. 200. Sorensen studies gave to serum albumin a value of 34.000. Colloidal theorist estimated a much lower molecular mass for proteins (around 5000). Olby, 1974, op. cit., pp. 8.

164 Olby, 1974, op. cit., pp. 4-5. Fruton, 1992, op. cit., pp. 111. Molecular theory was based on a precedent form, that of the 'polymer concept' proposed by Kekule who developed a classification system based on structural theory and the synthesis of organic substances in the lab.

(1884-1971) by using his own method of ultracentrifugation (analytical) was able to calculate their molecular mass and hence to be able to make a hypothesis on what the structure of the cytoplasm was.[165] The ultracentrifuged proteins separated, according to their molecular mass in well-defined fractions, indicating a uniform well-defined size for each of them (an aggregation of smaller molecules would have produced a continuous range instead).[166] Studies such as this gradually began to suggest that proteins like haemoglobin and serum albumin had molecular masses closer to those predicted by macromolecular theory.[167]

Also important for the decline of colloidal theory, since the theory denied its very possibility, was the realisation that, enzymes (proteins), after isolation and purification could be crystallised making them available for structural studies by X-ray crystallography.[168] This event constitutes the direct link to the development of 3D models of proteins (the second type of the second-generation models). These models were the result of the work of Linus Pauling (1901-1994), Robert Corey (1897-1971) and also Herman Branson (1914-1995).[169] Relying on the conceptual appliance of quantum mechanics to chemistry these authors proposed the existence, based on the idea of duality, of alternative and coexistent forms for a molecule ('resonances of structure'). This idea, for instance, was determinant for the proposal of the concept of 'planarity of the peptide bond', which gave rise to the field of structural biochemistry.[170] They

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165 Olby, 1974. op. cit., pp. 11-14. Fruton, 1999, op. cit., pp. 200.

166 Noel G Goley, *From animal chemistry to biochemistry*, (Bucks, Hulton Educational Publications, 1973, pp. 235.

167 These two were proteins were specially valued by Svedverg because of the data consistency on their molecular weight with that of others researchers. See table 2.1 in Olby 1974, op. cit., pp. 12.

168 Fruton, 1976, op. cit., pp. 333 (ref 43). Albuminoid substances (proteins) were defined as non-crystalline material.

169 Branson's role on the proposal of the $\alpha$ helix $\beta$ sheet structures for proteins is not mentioned in the majority of biochemistry textbooks. The historian of biology Judson argues that Branson's role deserves a greater credit that the one he got. (http://www.pnas.org/site/misc/classics1.shtml (Consulted on January 2010). The work of Corey, Pauling and Branson on the conformation that proteins take in space (secondary structure) started in the late 1940s at the Institute of Technology of California (Caltech) and culminated with the publication of a series of papers published in 1951.

170 The following reference is only one of the eight papers published on the structure of proteins. Linus Pauling, Robert B Corey & Herman R Branson, 'The structure of proteins: Two hydrogen bonded helical

reported two main forms for the secondary, spatial, structure of proteins, the α-helix and the β-sheet,[171] both based on the existence of a different type of bond to the covalent one between atoms, the hydrogen (weaker) bond.[172] More importantly, although of a weaker nature, the hydrogen bond made it possible to explain protein spatial conformations.[173]

It is important to emphasize that 3D spatial imagery, as paper formula, is also of a symbolic nature. Its symbolism would be pivotal for the fact that from that time onwards in the lexicon of cell biology the 'texture' of the cytoplasm began to mean 3D tangible molecules. They became for students and bio-scientists worldwide, not only tangible but also 'real' entities; entities that despite looking like billiard balls, they were taken to be 'real molecules'. The sense that 3D gave was that anyone could be able to witness their existence and even share a moment with them if needed. Corey and Pauling in fact got photographed standing close to their 3D models and even played with them on many occasions, allowing them to become iconic rather than symbolic (see chapter 4).[174]

The last visual form of second-generation models from the second wave of molecularisation of cell biology comprises the early models of molecular biology, that is, those developed as the result of the experimental work of molecular genetics

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configurations of the polypeptide chain. *PNAS*, 1951, 37: 235-40. The full list can be found at www.pnas.org/site/misc/classics1.shtml (consulted January 2010).

171 The α-helix was confirmed by X-ray crystallography experiments by Max Perutz (1914-2002) in 1951. See: David Eisenberg, 'The discovery of the α-helix and β-sheet, the principal structural features of proteins' *PNAS*. 2003. 100: 11207-210.

172 While the covalent bond involves a share of electrons of the outer orbit (valence electrons) from two contiguous atoms interacting with each other in a molecule, the hydrogen bond allows for atomic interactions in atoms from different locations in a molecule. This ideas on different types of chemical bonds were the main subject of Pauling's classic textbook: Linus Pauling, *The structure of the chemical bond and the structure of molecules and crystals*, Ithaca, New York, Cornell University Press, 1939.

173 The hydrogen bond, is due to the high polarity (different charge in the anatomy of the molecule) of some molecules. It is the one that holds molecules of water together. The two other types of weak bonds are Van der Wall forces and molecule ion attractions also based on the temporary polarisation of electrons in a molecule. Van der Wall bonds it is argued play a key role for the temporary on/off (interaction/non-interaction) states of signal transduction processes.

174 This sort of photographical encounter will become a sort of *cliché* . Later Max Perutz (1914-2002) posed close to 3D models of Hemoglobin, John Kendrew (1917-1997) to 3D models of myoglobin, and James Watson and Francis Crick (1916-2004) to the helical model of DNA.

(1930-1960) on bacteria and viruses. **(Figure 18 A)**, **(Figure 18 B, d,** see page 84 and 85 respectively**).** Three archetypal models of the third-generation are that of the double helix proposed by Watson and Crick for the structure of DNA, those of isolated ribosomes translating a messenger RNA into protein[175] and that of the operon model of gene regulation proposed by Jacob and Monod.

All these images have become in different measures symbols not only of structure but also of a mechanism and of an experimental proof of a theoretical model. As in the case of images of metabolic cycles, when these images featured in cytology/cell biology textbooks for the first time, they were part of special chapters either on the physicochemical composition of cells or about the new chapters devoted to the emergent field of molecular genetics.

### 1.2.3. The third-generation models: The visual forms of the third wave of molecularisation of cell biology (1970s to the present), from signal transduction to interactomes.

The third wave of molecularisation of cell biology is a process closely related to the latest phase of the epistemic expansion of the molecular paradigm in biology that began to take place from the mid 1970s.[176] This latest phase required many factors to occur. It depended and relied on, firstly, the application of previous accumulated knowledge on molecular genetics into eukaryotic cells, secondly, the development of new technologies, thirdly, the creation of a new working conditions in academia and finally the existence of a new type of scientific self as part of a new epistemic culture.[177] Soon

175 A model that when associated to cell structures such as the rough endoplamic reticulum and includes the process of molecular modification of proteins (maturation) becomes one of the third-generation (see the subsection that follows).

176 Morange divided the epistemic expansion of the molecular paradigm in two periods: A period of development of conceptual tools (1940-1965) and a period of operational control (1972-1980). Morange, 1998, op. cit., pp. 2.

177 Whilst the expansion of the molecular paradigm and the development of new technologies are discussed in this chapter, the emergence of new academic set ups and on the existence of a new type of scientific self, are issues discussed in Chapter 5.

after the emergence of DNA recombinant technology,[178] two of the findings of the molecular genetics classical period, the operon model and the allosteric model for gene expression in bacteria began to resonate in a different light to biologists.[179] The advent of this technology would allow the resolving of many resting issues.[180] Firstly, it became possible to set in motion the old aspiration of changing the fate of a living organism by changing its genes.[181] Secondly, it made possible to test experimentally if both models of genetic regulation were also a part of eukaryotic cells. In other words, if these mechanisms were universal to all forms of life, as Jacob and Monod wishfully expressed it in 1961, when they stated that 'all that is true for E-coli is true for the elephant'.[182] Thirdly, it allowed a molecular explanation of two key biological phenomena occurring in higher organisms (eukaryotes), namely, the change in genetic expression induced by hormones, and even more importantly, the process of cell differentiation, two complex cellular phenomena that had puzzled embryologists for a long time.[183]

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178 For more information on the emergence of DNA recombinant technology and genetic engineering see: Morange, 1998, op. cit., pp. 183-203. See also: Wright, 1994, op. cit., pp. 65-78.

179 These models were proposed by Francoise Jacob (1920- ) and Jaques Monod (1910-1976) and Jean-Pierre Changeux (1936- ) and Monod respectively. The Jacob and Monod operon model of genetic regulation showed that the expression of genes into proteins in bacteria was inducible. The Changeux and Monod allosteric model of enzyme regulation showed that bacteria enzymes could become active or inactive, depending on a regulatory substance fixing to its regulatory site by changing its spatial conformation. Morange, 1998, op. cit., pp. 150-163. See also: Morange, 2002, op. cit., pp. 12-15 and pp. 50-58.

180 This techne made it possible the manipulation of genes from eukaryotic cells; to eventually change (mutate) them outside those cells and re-introduce them in the same cells or others and look for phenotypic changes. As such alongside the techniques described in what follows helped to open a new world of experimental research lines on cells of higher organisms.

181 In his Nobel prize lecture of 1958 Edward Tatum (1909-1975) declared 'a more and complete understanding of the functioning and regulation of gene activity in development and differentiation […] may permit the improvement of all living organisms by processes which we might call biological engineering […] the biosynthesis of the corresponding nucleic acid molecules, and to the introduction of these molecules into the genomes of organisms.
See: http://nobelprize.org/nobel_prizes/medicine/laureates/1958/tatum-lecture.html (consulted February 2010).

182 The original in French reads: 'Tout ce qui est vrai pour le Colibacille est vrai pour l'éléphant'. From: Jacques Monod, Françoise Jacob, General conclusions: Teleonomic mechanisms in cellular metabolism, growth and differentiation, *Cold Spring Harbor Symposia on Quantiative Biology*, 1961, 26, pp 393.

183 The question of cell differentiation revolved around the following question. Why if all the cells from a multicellular organism have the same DNA and hence the same genetic information, are some genes active and some silent? For instance why does muscle not produce insulin as the β cells from the pancreas do. The idea of expansion of the molecular regulatory paradigm as found in bacteria to higher organisms was

Other research lines and technological developments chiefly from biochemistry and immunology were also involved in the third wave of molecularisation of cell biology.[184] Among the most important were studies on protein phosphorylation, on monoclonal antibodies, and on protein-protein interactions and techniques such as protein electrophoresis, antibody mediated Immunoprecipitation/Western blotting (IP/WB), and later the yeast two hybrid system.[185] The main visual form emerging from the third wave of molecularisation of cell biology, and key for the visual change **(Figure 18 A,** see page 84**)** are by-and-large those images of models of signal transduction and membrane embedded receptors with a signalling function and or macromolecular transport function (also those of protein synthesis and protein maturation associated to the membranes o the endoplasmic reticulum) **(Figure 18 B, e,** see page 85**)**. Essential for all the visual forms of the latest wave of molecular imagery especially for those of signal transduction events was the Jacob and Monod allosteric model of enzymatic action in prokaryotes, because of its capacity to 'visually embodying' the changes in protein conformation after interaction with other protein or substances and produce an effect (phosphorylation, protein translocation, etc).

Signal transduction imagery, the more important visual form of the third-generation models[186] aims to portray the different series of sequential and also simultaneous interactions among proteins that occur inside a cell soon after a receptor in its membrane interacts with its substrate. The substrate is normally conceptualised as a signal from other surrounding cells triggering a cascade of intracellular protein-protein interactions, many including post-transcriptional changes such as phosphorylations and

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originally proposed by Jacob and Monod at the end of the Cold Spring Harbor (CSH) meeting of 1959. Morange, 2002, op. cit., pp. 3-96 and pp. 35.

184 Some input from electron microscopy is undeniable for the case of images of translocation processes through membranes and of immunofluorescence based optical microscopy (protein co-localisation studies) for the imagery of signal transduction processes. Data of two proteins marked with different fluorochromes co localizing in a given sub-cellular structure, for example suggest that they are close to each other and could interact.

185 It arguably also has inputs from X- rays computerised structural studies of proteins.

186 Most important because of its quantitative and qualitative growth.

dephosphorylations, inside the targeted cell that drives it to alter its functioning in many ways, with many of these changes involving a change in gene expression.[187] The final cellular effect of this sequential cascade of intercellular molecular events is varied. It could entail changes of the internal metabolism, induction to produce other substances, promotion of cell division, or cell differentiation or even its death. Based on what they do during the process of signal transduction, embedded in a network, protein function ranges from receptors, mediators, relays, scaffolds, adaptors, bifurcators, transducers, amplifiers, integrators, anchoring, modulators, and messengers proteins.[188] As we will see in the next chapter, although this visual form emerged in a primordial form in the 1975 edition of CB **(Figure 19)**, it will in the different editions of MBC, that its number and complexity would become more significant.[189] Images of signal transduction processes in cell biology textbooks and articles have changed significantly through the years. The first images had a linear structure, with proteins interacting in a sequential manner to have a stimulating positive role in a given cellular event, such as growth. As the process gained in complexity because of new interactions being described experimentally the images began to include inhibitory interactions and simultaneous interactions apart from sequential ones.

Signal transduction imagery has kept growing in number and complexity in the successive editions of MBC **(Figure 20)**. This growth has also manifested in other sources such as scientific articles[190] and also in the brochures of biotech companies aimed at selling antibodies against proteins involved in several cellular processes **(Figure 21).**

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187 Carl-Henrik Heldin and Mary Purton, *Signal transduction*, London , New York, Tokyo, Melbourne., Madras, Chapman & Hall, 1996. Bastien D Gomperts, Ijsbrand M Kramer, Peter, E R Tatham, *Signal transduction*, Amsterdam, London, Elsevier Academic Press, 2002.

188 Alberts, et al. 2002, op. cit., pp. 844.

189 As Morange has noticed, although the notion of receptor as a mediator pre-dated molecular biology it was only after its development that ideas of internal signalling further developed. Morange, 1998, op. cit., pp. 180.

190 In the year 2000 12% of all papers published on cells also contained the expression 'signal transduction' in them. The number of papers published containing the term has increased from around 7 in 1980 to 10.000 in the year 2000. Gomperts, et al. 2002. pp. 2.

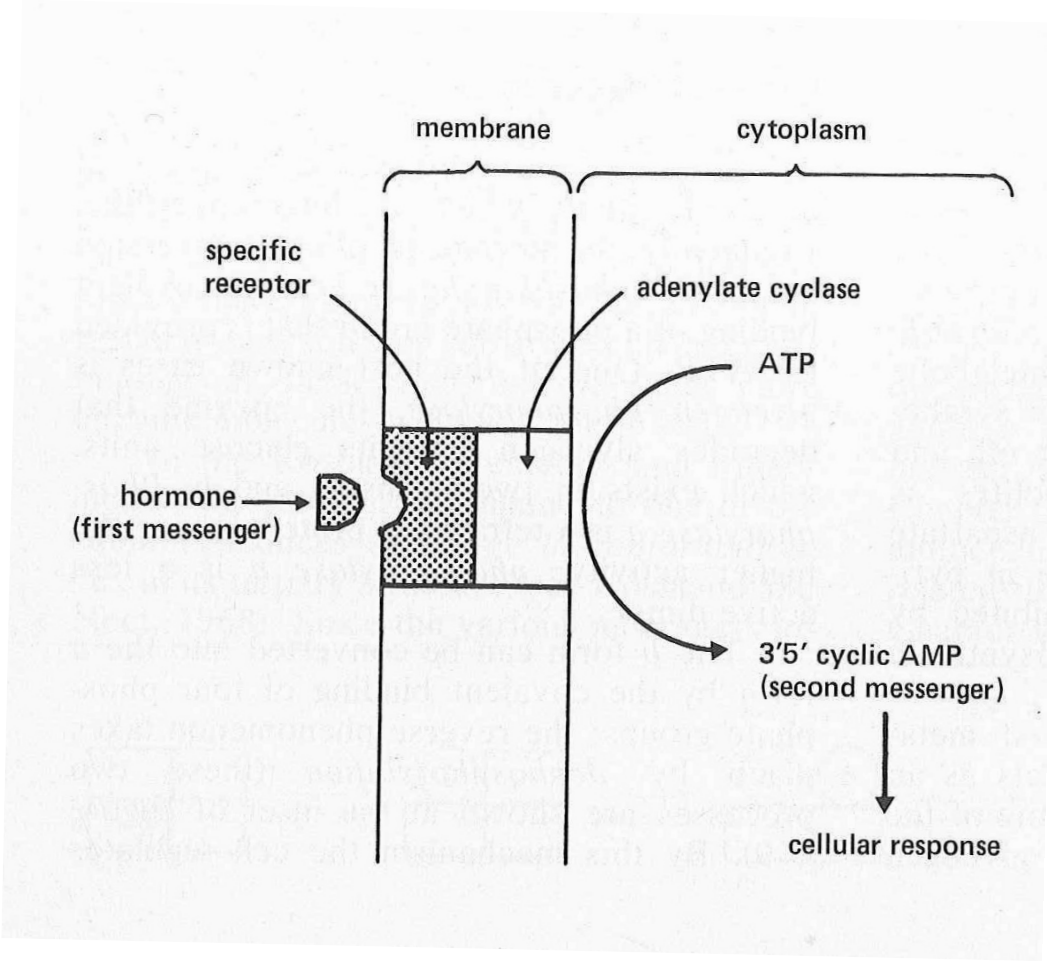
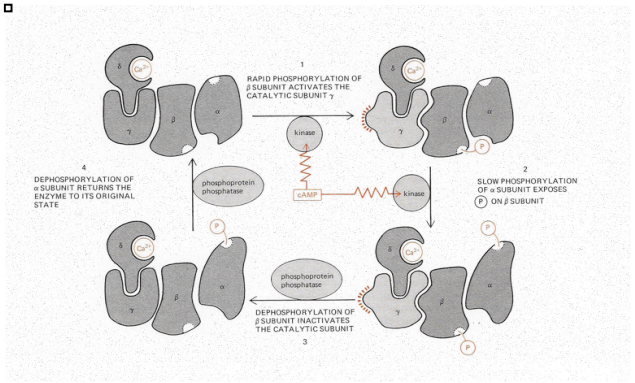
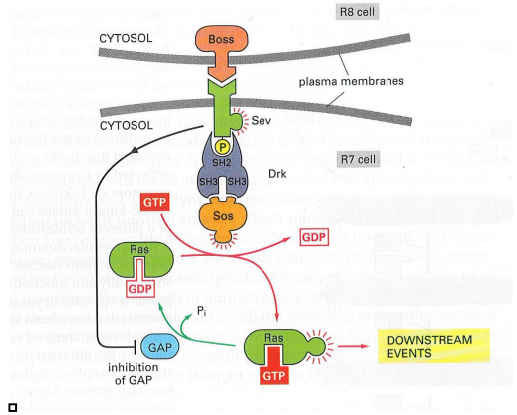


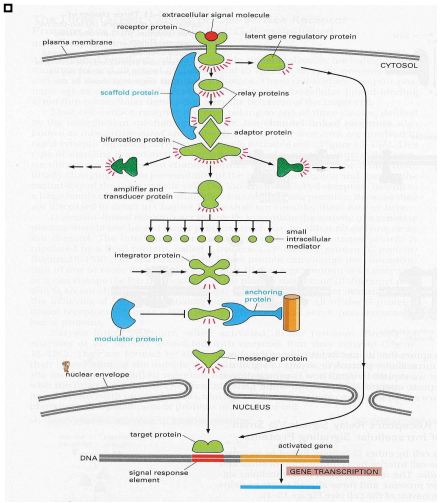

**Figure 19: The idea of signal transduction. De Robertis et al 1975**




1983




1994




2002

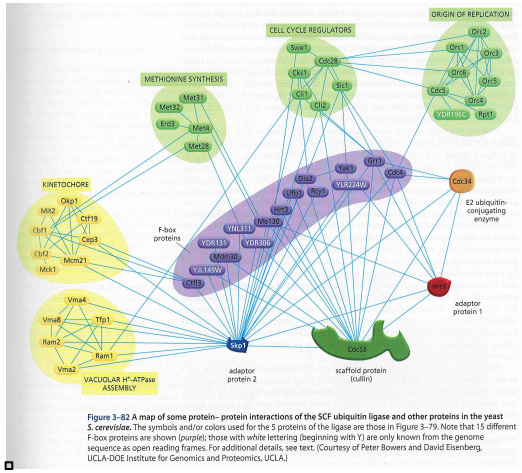



Figure 3–82 A map of some protein–protein interactions of the SCF ubiquitin ligase and other proteins in the yeast *S. cerevisiae*. The symbols and/or colors used for the 5 proteins of the ligase are those in Figure 3–79. Note that 15 different F-box proteins are shown (*purple*); those with *white* lettering (beginning with Y) are only known from the genome sequence as open reading frames. For additional details, see text. (Courtesy of Peter Bowers and David Eisenberg, UCLA-DOE Institute for Genomics and Proteomics, UCLA.)

2008

**Figure 20: The growth in complexity of signal transduction imagery through the successive editions of Alberts et al. MBC**

**Figure 21:** **Images of signal transduction pathways in biotech companies catalogs**

The latest manifestation of molecular imagery is that of the interactome **(Figure 22)**. Emerging in the 2000s, it builds on the images of signal transduction processes that began to appear in cell biology textbooks by the early 1980s. In contrast to them, the interactome has a greater and more 'global' objective, that of visually expressing in one 'snapshot' the total 'web' of all the possible protein-protein interactions occurring in a cell.

Signal transduction and interactomics are imagery fields *par excellence*. Their intelligibility is based on images and these images are the result of a process of translation, one in which one type of non-optical techne based visual output is converted into another (**Figure 23, left and right respectively**).[191] Signal transduction studies are by and large based on the interpretation that the traces (black dots in an autoradiograc film) left by a macromolecular complexes detected in autoradiographic films, are the result of proteins interacting in cells. A brief account of the IP/WB technique main features in what follows will suffice to give us an idea of how the process of translation of images works. The process starts by separating all cellular proteins from other molecules such as DNA after the maceration of tissue in a detergent based medium and successive steps of centrifugation. The proteins contained in this cellular homogenate after interaction with and antibody specific for one of those proteins (protein 1) are separated according to their molecular weight by electrophoresis. The proteins separated according to their molecular weight are then transferred to a membrane by a techique known as Western Blotting (WB) and exposed to another antibody against protein 2 (a protein that is assumed to be interacting with protein 1) which because its linkage to a light emitting molecule is detected in a radiographic film **(Figure 23, left)**. A black signal on the radiographic film is taken as proteins 1 and 2 interacting in the cell **(Figure 23, right)**. The intensity of the signal in the autoradiogram is taken to relate to the amount of proteins 1 and 2 interacting.[192]

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191 As somehow for all the other cases of molecular imagery the difference resides in different processes of translation.

192 For some details on these techniques and others used to study the interaction of proteins in signal transduction processes, such as Yeast Two Hybrid System (YTHS) see Alberts, et al. 2008, op. cit., pp. 517-24. Since the interaction between proteins in many instances depends on the reversible phosphorylation of proteins on the aminoacids Tyrosine and Serine, signal transduction experiments may

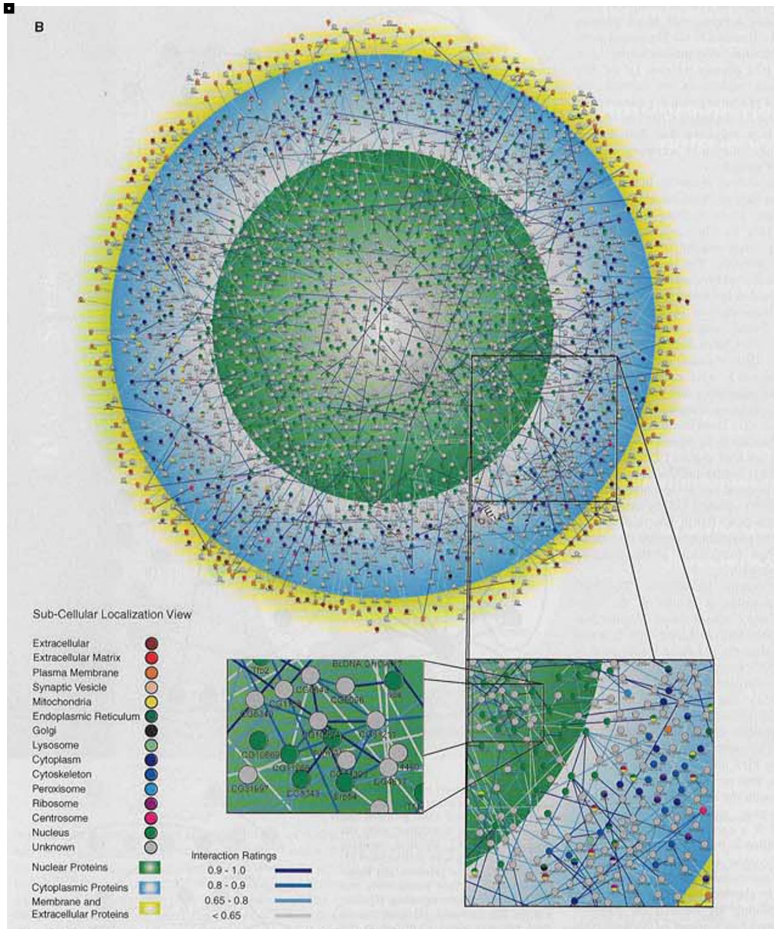


**Figure 22: The interactome. Giot. L, et al. Science 302. (2003)**

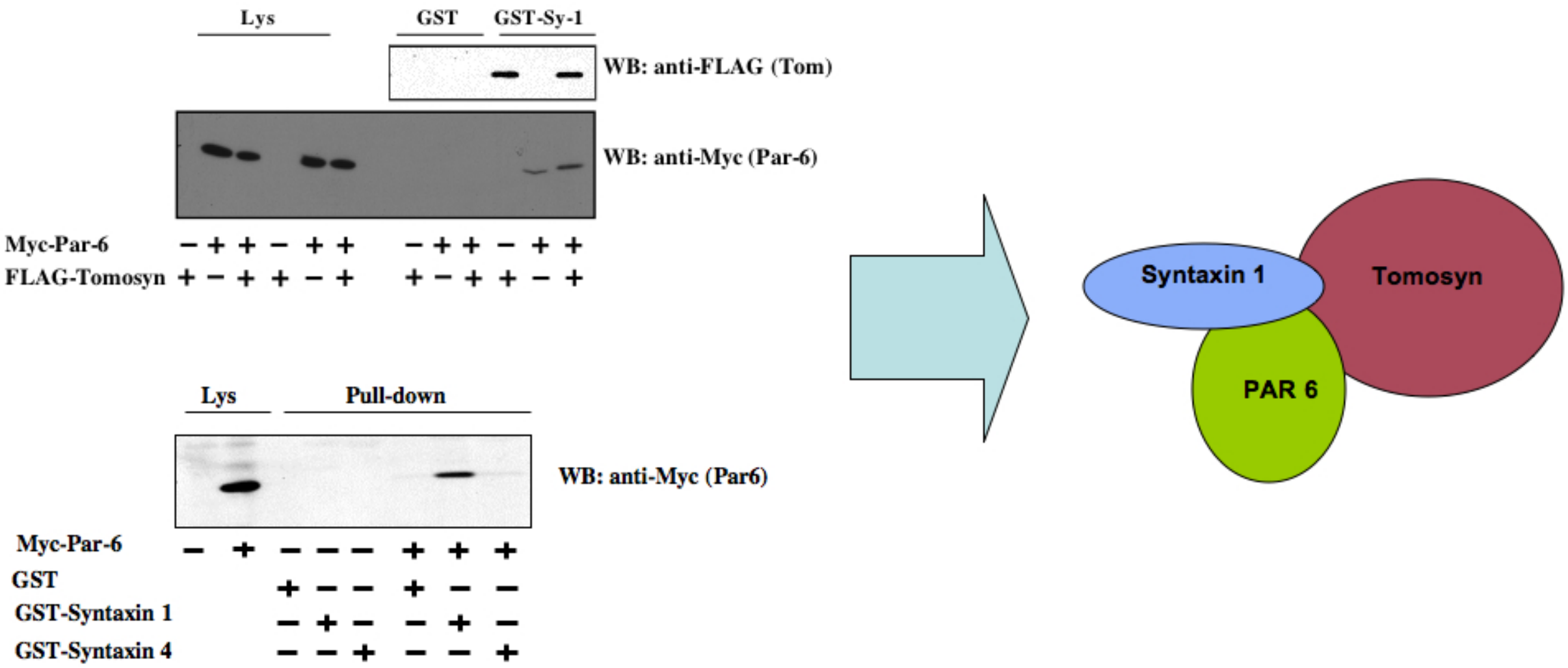


**Figure 23: Process of visual translation of molecular imagery of the 3rd order. Signal transduction imagery is constructed by the visual translation of the 'traces' left by molecules in an autoradiogram (left). Serpente, unpublished data**

Having classified the images contained in cell biology textbooks, identified the two more prominent ones involved in the visual change (the microscopical and the molecular) and discussed their main features, it is time now to move into next chapter to discuss why this dissertation selected textbooks as the main sources to study this visual change.

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involve extra experimental steps to induce and then to determine the phosphorylation state of proteins containing these aminoacids.

## Chapter 2. Tracking the visual change in textbooks (1940s-2000s).

### 2.1. Why textbooks?

One central argument of this dissertation is that textbooks are the main medium in which the visual change in cell biology manifested. Why focus on textbooks and not on other sources such as scientific articles, which also acted and continue to act as carriers of the two types of images (microscopical and molecular) involved in this change? Historians, scientists, and lay people would all agree that textbooks are central for the production of knowledge in scientific disciplines. This view although correct needs examination, for it risks disregarding specific ways by which through history textbooks become pivotal for the establishment of new, epistemic and in particular visual conditions. To avoid this a more comprehensive view is required, one that firstly historicizes the production of textbooks and the production of knowledge and, secondly, one that explores the relationship of textbooks with the enactment by scientists of the knowledge practices at the educational level in universities and at the experimental level in laboratories.

Thomas Kuhn (1922-1996) was one of the first historians/philosophers that has attempted to piece together these two issues. Kuhn argued that the achievements accumulated during 'normal science', such as the description of accepted theories together with 'exemplary observations and experiments' for a given discipline are contained in textbooks.[193] In Kuhn's diachronic view of science with periods of normal science alternating with revolutionary ones, textbooks become carriers not of universal, but ratherof temporal truths. Despite that temporal validity, textbooks are powerful enough to 'address themselves to an already articulated body of problems, data and theory, most often to the particular set of paradigms to which the scientific community is committed at the time they are written'.[194] As such, textbooks, not only provide students with a set of initial 'intellectual foundations', that they will carry with them to solve

193 Kuhn, 1970. op. cit., pp 10.

194 Ibid. pp. 136. Kuhn also argued that textbooks alongside popularizations and works on philosophy of science are the sources from where science gets its authority (Ibid.).

specific problems later in their professional lives but will continue to provide 'route maps' once they become independent researchers.[195] Already as professionals they will browse for directions on topics that suddenly become forgotten or for guidance on new experimental routes to take. Taken as a whole these are the main reasons why cell biology textbooks have been selected to study the visual change. One extra reason for this selection relates to their duality at exposing very recent and simultaneously quite well established 'advances' in a particular area of knowledge. When compared with scientific articles the epistemology carried in textbooks is assumed to be less hypothetical, quite well established, better probed experimentally and hence of a more permanent nature.[196]

Two textbooks were selected for this study. The first one is *Molecular Biology of the Cell* (MBC), which was first published in 1983 by Bruce Alberts, Dennis Bray, Julian Lewis, Martin Raff, Keith Roberts and James Dewey Watson. MBC has a total of five editions up to present. The second (1989) and third (1994) editions, with the same set of authors, and a fourth (2002) and fifth (2008) authored by Bruce Alberts, Alexander Johnson, Julian Lewis, Martin Raff, Keith Roberts and Peter Walter. The second textbook selected is *General Cytology*, first published in English in 1948 (original in Spanish, 1946) by Eduardo P D De Robertis, Francisco Saez and Wiktor Nowinski. *General Cytology* has a total of eight editions, the second (1954), the third (1960) and the fourth (1965) with the same set of authors. The fifth edition (1970) has the same authors, but it changed its title to *Cell Biology* (CB). The sixth edition (1975) kept the same title but was authored by Eduardo D P De Robertis, Francisco A Saez and Edward M De Robertis (Eddie De Robertis). The seventh (1980) and eighth (1987) editions were published under the name of *Cell and Molecular Biology* and were co-authored by Eduardo D P De Robertis & Eddie De Robertis.[197] Whereas my analysis include all the editions of MBC, only six out of the eight editions published (1948, 1960, 1965, 1975, 1980 and 1987) of

195 Gaster, Barak, 'Assimilation of scientific change: The Introduction of molecular genetics into biology textbooks', *Social Studies of Science*, 1990, 20:3, 431-54, pp. 431.

196 As we will see later in Chapter 3 on the making of MBC this was not always the case.

197 To avoid confusion do to with the diversity of titles and changing authorship in the textbooks assessed, I use 'MBC' and 'CB' or sometimes Alberts' et al and 'De Robertis, et al, respectively to generically refer to each textbook, following by the year of publication of each edition when required.

CB were surveyed, since that of 1954 has almost no changes when compared with the preceding one, and that of 1970 was not available.

Although already anticipated in the introduction of this dissertation it is worth recalling briefly here the reasons behind the choice of these textbooks as primary sources. The focus on MBC is because this textbook was the printed media where by and large the visual change began to manifest. In many ways MBC can be considered as a watershed in the discipline. This, not only because, as I will show Chapter 3, it exhibits novelty in its making, but more importantly because, MBC was the main medium that began to profusely create and display the latest form of molecular imagery to students. Briefly stated, MBC is a product of the molecular culture as opposed to the microscopical one (see Chapter 5). That said, from an historical perspective, such as the one taken in this study, the molecular imagery displayed in MBC does not make too much sense on its own. It has to be compared with the imagery that preceded it. CB, is the perfect source to achieve this comparison mainly because in contrast with MBC, it belongs to the microscopical tradition; this, as we will see later, even after different attempts of molecularising the textbook (especially from the 1975 edition when Eddie De Robertis, a molecular biologist co-authored it). Moreover CB is the most suitable source to compare with MBC because, firstly, since it first appeared (as *General Cytology* in 1948) and for many years (circa up to 1970) it was the textbook that not only contained the largest number of images per page, but also these images were of a diverse nature.[198] Secondly, its two latest editions, those of 1980 and 1987 overlapped for a period of four years with the first edition (1983) of MBC. Two extra characteristics, shared by CB and MBC, make them suitable sources for analysis. Firstly, it is possible to recognize common themes in the different chapters from all the editions assessed of both textbooks. Secondly, CB and MBC were in their times two of the most popular textbooks for university students of the biosciences not only in the USA and Britain but also all over the world as the translation to the different languages of both treatises suggests.

198 Examples of textbooks containing far less number of images than De Robertis, et al are those of: Brachet and Mirsky, (1959-1961). op. cit., R A R Gresson, *Essentials of general cytology*, Edinburgh, Edinburgh at the University Press, 1948.

It should be stated that MBC and CB were not the only textbooks in cytology/cell biology that existed throughout the period surveyed (1940-2009). In fact many other textbooks coexisted with them and had relevance for the discipline. None of those textbooks however are considered in my study mainly for two reasons. Firstly, many had only one or two editions in the period considered, sometimes even not fully overlapping with those of MBC and/or CB. Secondly, as anticipated earlier, many of them contained a small number of images and/or have both microscopical and molecular issues located in different chapters. To give some concrete examples: Brachet's and Mirsky's *The Cell*, was a highly valued textbook in cell biology, but it was directed to a more specialised reader, it has only two editions and it contained a low number of images, with this number remaining almost unaltered in both editions.[199] Other examples reviewed are: A) Kimball's *Cell Biology*, a textbook that in its three editions (1970, 1978 & 1984), has a dominant imagery based only on microscopical images which in addition was located in different chapters to those in which molecular images were displayed.[200] B) Dyson's *Cell biology a molecular approach* (1978), which had only one edition and its visuality is by and large based on drawings and images obtained with microscopes.[201] C) Fawcett's *The cell*, a textbook that despite its quality and its popularity among medical students is based almost entirely on images obtained with the electron microscope.[202] D) De Duve's *A Guided tour of the living cell* a textbook, which although of impressive quality was very introductory and hence targeted to the wider public or at most to high-school students; De Duve's also had only one edition.[203] Finally, there is the book by Haggis et al *Introduction to molecular biology*, [204] a book that in spite of its title is about cells had

199 Brachet, et al. (1959-1961), op. cit.

200 John W Kimball, *Cell biology*, California, London, Sidney, Addison-Wesley Publishing Company Inc, (1970, 1978 & 1984).

201 Robert D Dyson, *Cell biology a molecular approach*, Boston London Sydney Toronto Allyn and Bacon, Inc, 1978.

202 Fawcett, (1966 & 1981), op. cit.

203 Christian de Duve, *A Guided tour of the living cell, (vols. 1 and 2)* New York, Scientific American Books in Collaboration with Rockefeller Univeristy Press, 1984.

204 G H Haggis, D Michie, A R Muir, K B Roberts & P M B Walker, *Introduction to molecular biology*. London. Longmans Green and Co Ltd, 1964.

only one edition and both imageries, microscopical and molecular were located in different chapters.[205]

A first basic notion on the differences between MBC and CB could be obtained from a glimpse at the numbers provided in **Figure 24.** A comparison of the ratio of images per page and the average number of figures per chapter for each edition of both textbooks clearly shows not only that MBC was a more 'visual' textbook than CB, but also how visual the discipline had become in a period of circa 50 years. So, whereas from the 1950s to the early 1980s (De Robertis' et al case) the number of images per page was less than one, from the early 1980s (Alberts' et al case), this number almost doubled, with on many occasions when a given page containing more than one image.

### 2.2. How textbooks on cells looked at the outset of the 20th century.

As I anticipated in Chapter 1, the discipline that preceded cell biology, cytology, began to emerge as a relatively consistent body of knowledge many years after cell theory. The process was not at all straightforward and only after steering clear of many conceptual and experimental difficulties, did cell theory gain widespread acceptance in universities and research centres all over Europe.[206] This was a time, circa the 1890s and coincided with the emergence of 'cytology' as a scientific discipline. The three main textbooks on cells produced before that time were: for the US and English speaking world, Edmund B Wilson's, *The cell in development and inheritance* (1896-1900), for the German language Oscar Hertwig's, *Zelle und gewebe* (1893) and for the French, Louis Felix Hemeguy's, *Leçons sur la cellule* (1896).[207] What all these treatises on cells have in common is that all the epistemic arguments on cells were mostly based on microscopic imagery, at the time the only imagery present in textbooks. Cells were essentially observed with a light microscope and their images then depicted either directly with the

205 This textbook was viewed by Keith Roberts as an example not to follow when producing MBC (see chapter 5).

206 Hughes, 1959, op. cit. (see chapter 4).

207 In what follows I will begin from and base my account on Wilson's treatise an as such focus on the science of cytology later named cell biology as produced in the English speaking world.

## De Robertis et al Cell Biology

| Publication Years | 1948 | 1960 | 1965 | 1975 | 1980 | 1987 |
|---|---|---|---|---|---|---|
| Total numbers of pages | 345 | 555 | 446 | 615 | 647 | 734 |
| Total numbers of Images | 143 | 253 | 290 | 360 | 421 | 487 |
| Ratio (Images/Pages) | 0.41 | 0.45 | 0.65 | 0.58 | 0.65 | 0.66 |
| Average of Figures/ Chapter | 11.9 | 15 | 13 | 14 | 15 | 20 |

## Alberts et al Molecular Biology of the Cell

| Publication Years | 1983 | 1989 | 1994 | 2002 | 2008 |
|---|---|---|---|---|---|
| Total numbers pages | 1146 | 1218 | 1294 | 1463 | 1601 |
| Total numbers of Images | 1284 | 1463 | 1434 | 1713 | 1819 |
| Ratio (Images/Pages) | 1.12 | 1.20 | 1.11 | 1.17 | 1.14 |
| Average of Figures/ Chapter | 68 | 70 | 60 | 69 | 73 |

**Figure 24: The changing balance between images and text in cell biology textbooks 1940s-2000s**

*camera lucida*, or by drawing them from daguerreotypes. Most of the observations were done at the time with as little intervention as possible to avoid compromising the cell's integrity and to adhere to the canons of a regnant 'mechanical objectivity'.[208] Based on the idea of mimesis these observations aimed to produce an image that faithfully reproduced the cell as object (see discussion on this issue in Chapter 4).

Wilson's treatise in particular was central for the conformation of cytology as a scientific discipline. Whilst the first two editions (1896-1900) were determinant for the final establishment of cell theory, the third edition of 1925 was determinant for the entry of Mendel's laws of inheritance in cytological studies, a thematic area that would later derive in the sub-discipline of cytogenetics.[209] Key for the final acceptance of cell theory was Wilson's position in his book of keeping 'the cell at centre stage', that is, considering the cell as an "organism" in its own right involved in biochemical genetic and developmental processes. Wilson's position was due to his firm belief in a more holistic notion of what life is, one based on the German concept of 'Zellforschung'. In practice 'Zellforschung' entailed the observation of cells as part of a program of experimentation that had as a philosophical bedrock assumption the aspiration to furnish a universal answer to the 'secrets of life'.[210] Microscopical images were paramount for both Wilson's commitment to keep 'the cell at centre stage' and for the creation of a 'visual regime' that eased the process of perception of images by making them refer 'to prior schemata and concepts'.[211] One important issue to retain at this point is that Wilson's 'visual regime' in *The Cell* would set the tone for most of the main themes and imagery

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208 Daston, et al. 2007, op. cit. Mechanical objectivity in the form of photography was a key epistemic virtue that emerged at the end of the 19th century allowing cytologists to believe that by cultivating its practice the inference of subjective visions would be avoided and thus 'real' knowledge about cells could be attained.

209 Mainschein describes an increase in abstract depictions and interpretative forms (rather than descriptive ones), through the successive editions of Wilson's treatise, especially when he began to incorporate the Mendel laws of heredity. Jane Maienschein, 'From Presentation to Representation in E. B. Wilson's *The Cell', Biology and Philosophy*, 1991, 6: 227-54.

210 Ariane Dröscher. 'Edmund B. Wilson's the cell and cell theory between 1896 and 1925'. *History and Philosophy of The Life Sciences*, 2002, 24: 357-89, pp. 359-60. 'Zellforschung' was the practice pioneered by Richard Herwith, Max Verworn and Theodor Boveri, the later by whom Wilson was highly influenced.

211 Jacyna, op. cit., pp. 77.

that subsequent textbooks on cells began to exhibit for the first 50 years of the 20th century, including of course De Robertis et al CB.

### 2.3. The case of De Robertis et al Cell Biology: An exemplar of the microscopical tradition for the 20th century.

The third edition of 1925 was the last to appear of Wilson's classic. Despite this, the book would have a long lasting effect on influencing newcomers to the discipline throughout the 20th century.[212] An important question arises at this point. How long would the 'visual regime' based on microscopical imagery established by Wilson's treatise last? An answer to this question is attempted by comparing the number of images of a microscopic and of a molecular nature that featured first in all the editions of CB,[213] a textbook that came to some extent to fill the vacuum left by Wilson's cytological treatise for a considerable part of the 20th century (from circa the1950s to the 1980s), [214] and secondly, in all editions of MBC, the textbook that heralded the process of molecularisation of cell biology (see the next chapter).

Of relevance for the temporal evaluation of the presence of microscopical and molecular imageries in textbooks is to have a numeric idea of the different types of images displayed in the different editions of both CB and MBC. With this in mind five categories for this quantitative analysis were created. The previous categories, 1-2-4-5-6

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212 In the preface of the second edition, the authors of MBC for example, cited Wilson's famous dictum that 'the key to every biological problem must finally be sought in the cell', in an attempt to justify their own book as having an epistemic historical connection with that of Wilson, the celebrated author who put cells at centre stage. Bruce Alberts, Dennis Bray, Julian Lewis, Martin Raff, Keith Roberts, James D Watson, *Molecular biology of the cell*, New York, London Garland Publisher Inc, 1989, pp. 5.

213 Eduardo D P De Robertis, Wiktor W Nowinski, Francisco A Saez, *General cytology*, Philadelphia, London W. B. Saunders Company, (1948, 1965, editions).
Eduardo D P De Robertis, Francisco A Saez, Eduardo M F De Robertis (Jr), *Cell biology*, Philadelphia, London, Toronto W. B. Saunders Company, 1975. Eduardo D P De Robertis, Eduardo M F De Robertis (Jr), *Cell and molecular biology*, Philadelphia, W. B. Saunders College, (1980 and 1987 editions).

214 Two textbooks that were published between Wilson's last edition (1925) and De Robertis', et al first one of 1948, they were: Lester W Sharp, *An introduction to cytology,* New York, Mc Graw-Hill Book company Inc, 1926. And, James C Gray, *A textbook of experimental cytology*, Cambridge, Cambridge at the University Press, 1931. Also relevant was Charles E Walker, *The essentials of cytology: An introduction to the study of living matter*. London, Archibald Constable & Co LTD, 1907.

(see Chapter 1) were relabeled respectively as follows: (1) Images obtained with a light microscope, (Light microscope, light blue bar), (2) Images obtained with an electron microscope (e- microscope, dark blue bar), (4) Images of cellular models (yellow bar), (5) Images created from electron micrographs (e- based models, orange bar), and (6) Third-generation of models of molecular nature (red bar). Full details on the quantification procedure are given in Appendix I. Whilst the conclusions of the quantitative analysis for CB are discussed in what follows, those for MBC are discussed in the following chapter.

CB was one of the most if not the most popular cytological treatises between the late 1940s and the early 1980s. This is manifested among other factors by its wide use in different biosciences-related courses across different universities in the USA, Europe and other parts of the world. In fact, encouraged by the enormous success the original 1946 edition in Spanish had at South American universities the book was first translated into English in 1948 and subsequently translated into many other languages. CB was translated to Portuguese and French from the first edition onwards, to Hungarian, Japanese, Italian, and Russian from the second edition (1954) onwards and to Italian and German from the third edition (1960) onwards.[215] This, sort of, 'best-seller' status, constituted a rare but significant achievement for a book of this kind at the time.[216] De Robertis, Nowinski and Saez produced a textbook that in their own words was one that presented readers interested in cytology 'with established facts'[217] and that 'tries to interpret and translate into didactic terms the extraordinary advances made by modern cytology'.[218] The authors of CB viewed their book as one 'intended primarily for college and courses in cytology and for students who, for purposes of teaching and investigation

215 Information obtained from the different editions of De Robertis, et al.

216 I could not find in my survey any other textbook on cell biology from the 1940s to the 1970s that was translated into so many languages. Only MBC would be translated into so many other languages many years later.

217 De Robertis, et al. 1948, op. cit., pp. iv.

218 De Robertis, et al. 1960, op. cit., pp. vii.

in other fields of biology such as medicine, genetics, physiology, agronomy or veterinary medicine wished to obtain a general view of some aspects of modern cytology'.[219]

The first edition of CB was positively reviewed. One reviewer described it as: a 'very meaty and condensed' treatise, where, 'the information is carefully presented' and 'clearly stated', a textbook that was written in a 'clear and readable style'.[220] Moreover, an advertisement page by its publishers, W. B. Saunders Company, in the scientific journal *Science* stated that the book 'included among the illustrations […] some of the finest electromicrographs ever published'.[221] Very precious words for an audience of cytologists eager to learn how to properly visualise the new images of cells that the electron microscope began to deliver at the time (see Chapter 1 on the interpretation of the electron microscope images). In effect CB was one of the first textbooks containing the new imagery promising to deliver the 'ultra structure' of cells (content and texture) 'beyond fixation and staining' to wider audiences.[222] What is more, when compared to other treatises of the time, De Robertis et al, is also the one that contained by far the largest number of images.

Previous to and up to the first edition of CB in 1948 the authors, De Robertis, Nowinski and Saez extensively used the optical microscope, as the main instrument for the production of images of cells. In the first edition, up to 28.15 % of the total amount of images contained in the book were produced with the optical instrument (light blue bar in **Graph 1**), exceeding the percentage of images obtained with the electron microscope (dark blue bar), that at the time only began to be used by the authors (17.80 % of the total).[223] Later, because of the authors' commitment to the use of the electron microscope to undercover the ultra-structure of cells, from the 1950s onwards this situation would

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219 De Robertis, et al. 1960, op. cit., pp. vi.

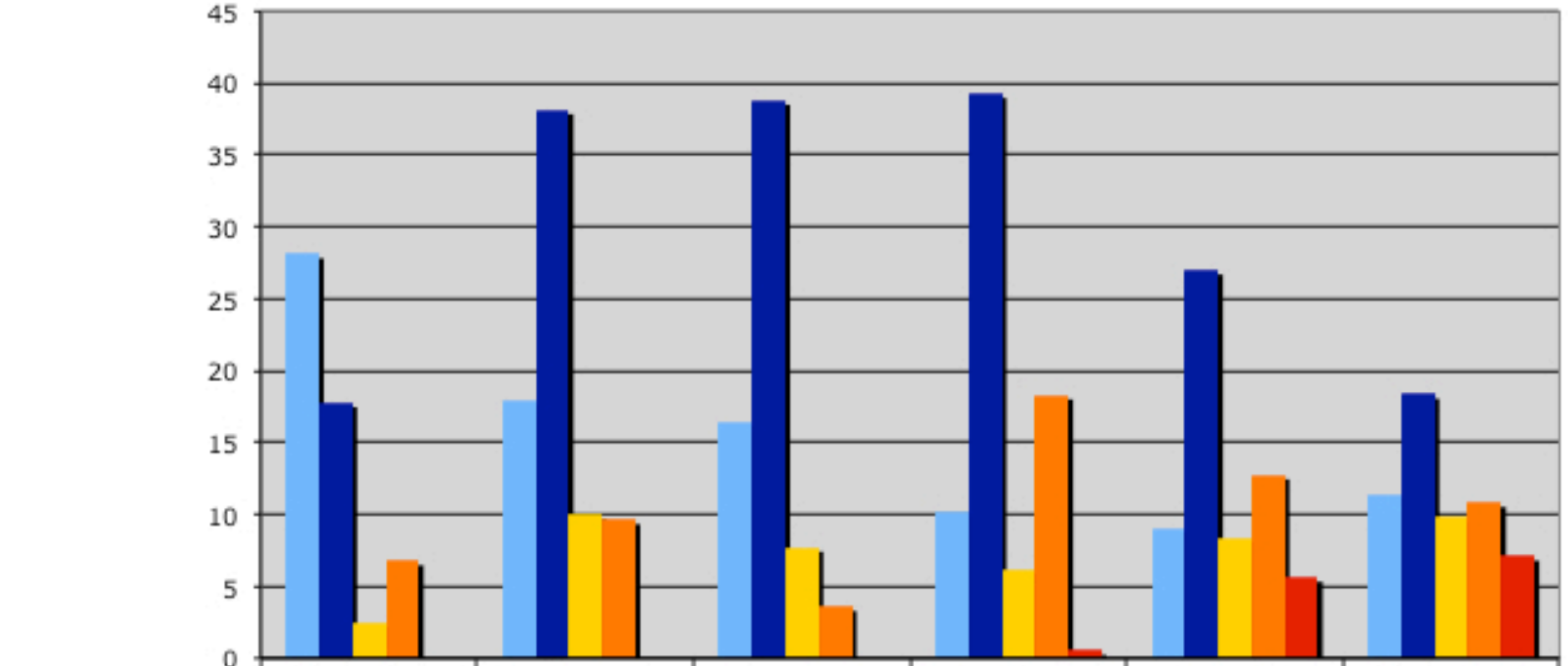
220 Anonymous reviewer of De Robertis, et al. 1948 in The Anatomical Record, 1948, 108: 333-4.

221 Publisher advert in *Science*, August 20, 1948, 108: 1.

222 Ibid.

223 For details on the construction of tables (raw data) and graphs see Appendix subsection A.2. *'Quantitative analysis of textbooks'*.

## GRAPH 1 De Robertis et al




| | 1948 | 1960 | 1965 | 1975 | 1980 | 1987 |
|---|---|---|---|---|---|---|
| light microscope | 28.15 | 17.9 | 16.48 | 10.16 | 9.02 | 11.42 |
| e-microscope | 17.8 | 38.17 | 38.82 | 39.3 | 27.02 | 18.39 |
| cellular models | 2.52 | 9.99 | 7.75 | 6.2 | 8.42 | 9.78 |
| e- based models | 6.81 | 9.67 | 3.63 | 18.34 | 12.78 | 10.86 |
| Molec. 3rd gen | 0 | 0 | 0 | 0.57 | 5.66 | 7.13 |

**Publications Years**

revert.[224] In the third edition (1960) this relation is radically inverted; the number of images produced with the electron microscope reached 38.17% of the total compared with 17.90% of images obtained with the optical instrument. Overall, the number of images over the total obtained with the optical microscope decreased from that edition reaching its lowest level in the 1980 edition (9.02%). In fact the electron microscope remained the main image producing technology in CB until 1975 when the images obtained with the instrument reached its maximum value, that of 39.30% of the total number of images in the book. Throughout all the editions the percentage of images obtained with the electron microscope remained higher than any of the other categories assessed. This even when its number began to diminish considerably in the 1980 edition to a 27.02% of the total and reaching its minimum in the 1987 edition when that value was of a 18.39% **(Graph 1,** see page 114**)**.

The quantitative analysis **(Graph 1,** see page 114**)** made of the different editions of CB clearly shows that the percentage of microscopical images together (light microscope + $e^-$ microscope) easily exceeded all the other categories assessed, (cellular models, $e^-$ based models and other molecular models) especially until the 6$^{th}$ edition of 1975. Taking this edition, for instance (the first edition that exhibits images of molecular models of the third-generation) microscopical images as a whole represents a 49.46% (10.16% of light microscope + 39.30% of $e^-$ microscope) of the total number of images displayed. Almost the double when compared with a 25.11% of images carrying models (6.2% cellular models + 18.34% $e^-$ based models + 0.57% molecular models of third-generation). It is only in the latest edition of 1987 (an edition that was produced at the peak of molecularisation and 4 years after the publishing of MBC in 1983), that the sum of all types of models by reaching a 27.77% (9.78% + 10.86% + 7.13%) of the total number of images almost matches that of microscopical images, which reached its lower level, 29.81% (11.42% + 18.39%).

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224 They become sort of pioneers on the use of the electron microscope on cytology and also lead the way in the combined use of this instrument together with the ultracentrifuge to investigate the localisation of the biochemical reactions that were reported to occur inside cells. See Chapter 1, subsection 1.1.2 *'The expansion of microscopical imagery: the electron microscope'*.

Another important feature that emerges from the quantitative analysis of the images displayed in the different editions of CB **(Graph 1,** see page 114**)**, and that would be relevant to compare with the figures from MBC (see Chapter 3, **Graph 2,** page 117), is the following: Images of cellular models (yellow bar) with the exception of the first edition of 1948, reached an almost 10% of the total number of images (9.99% of the total number of images in the 1960 edition) and then after a period of relative stagnation in the 1965 and 1975 editions (7.75% and 6.20% respectively) it began to grow again in the 1980 edition (8.42%) to reach a value of 9.78% in the 1987 edition. It is important to mention here that through the successive editions of CB, images of cellular models, especially in its two latest editions gained in detail and complexity.

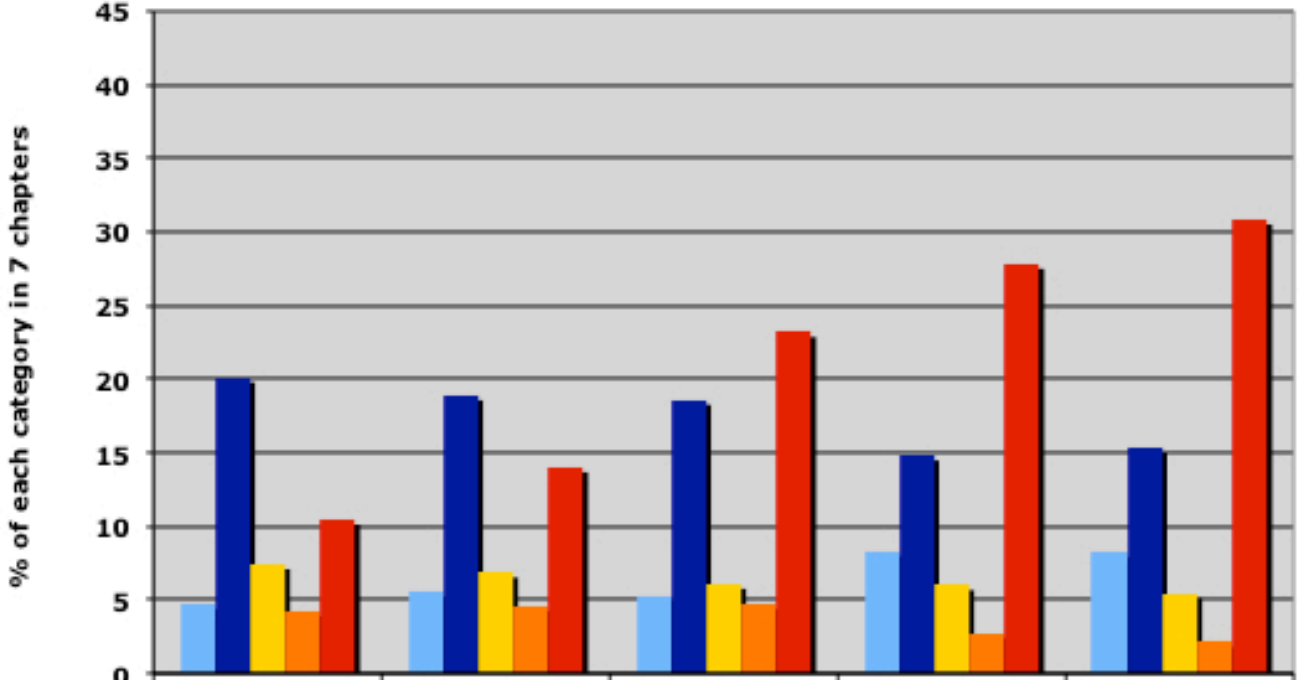
The percentage of images containing models based on the electron micrographs ($e^-$ based models, orange bar in **Graph 1, (**see page 114), not surprisingly, follows the variation of the percentage of the images (raw images) obtained with the instrument ($e^-$ microscope, dark blue bar, throughout the successive editions of CB. As anticipated earlier, images containing molecular models of the third-generation began to feature in the 1975 edition of CB representing only a 0.57% of the total number of images in that edition. They increase to a 5.66% in the 1980 edition reaching a 7.13% in that of 1987. It is important to notice that in all these three editions images of molecular models of third-generation (red bar) were lower in number than cellular ones (yellow bar), **(Graph 1,** see page 114**)**.

### 2.3.1. The development of molecular imagery inside CB: Some relevant aspects of its visual and epistemic content before the third wave of molecularisation of cell biology (1940s to the 1970s).

Concerning the relationship between imagery and knowledge production the following is relevant. For the editions of 1948, 1960, 1965 and 1975, images of cellular models went hand-in-hand with a cellular based epistemology, one that almost completely excluded molecules to explain the different aspects of cell behaviour.[225]

225 The only exception to this is the case of synaptic transmission where molecules such as acetylcholine were used to explain it.

## GRAPH 2 Alberts et al




| | 1983 | 1989 | 1994 | 2002 | 2008 |
|---|---|---|---|---|---|
| light microscope | 4.68 | 5.5 | 5.29 | 8.3 | 8.22 |
| e- microscope | 20.12 | 18.9 | 18.6 | 14.81 | 15.34 |
| cellular models | 7.42 | 6.86 | 6.09 | 6 | 5.47 |
| e- based models | 4.23 | 4.57 | 4.69 | 2.75 | 2.12 |
| Molec. 3rd gen | 10.45 | 14.01 | 23.2 | 27.84 | 30.85 |

Publications Years

These included themes such as the transport of secretory vesicles during the secretion of neurotransmitters, the dynamics of the vacuolar system, and the evolution of the Golgi apparatus, all instances including models of cells or cell particles to explain changes on the cellular state.[226]

Although the period between the 1950s to the 1970s was characterised by the extent and importance given to cellular explanation in cytology as manifested in CB, it is possible to distinguish the development of a molecular epistemology as a form of complementary explanation inside the discipline.

Apart from the case of synaptic transmission, De Robertis' own research subject, where molecules such as acetylcholine were used to explain it, the other clearest form of molecular explanation appeared in the 1960 edition of CB. In it cell permeability, the passage of a particle (mainly ions) from the outside to the inside of the cell, was reported to depend on a previous interaction with a 'substance' in the cell membrane allowing its move across it and hence allowing for its internalisation.[227] Likewise, amoeboid motion was explained as changes occurring in the network of proteins, more specifically due to conformational changes between fibrilar and globular structures.[228] Nevertheless, these with the exception of synaptic transmission, were only written attempts at describing molecular mechanisms, none of them included any kind of visual form. The description of the process of molecular mediated cell permeability, correspond to the current one on 'internalising receptors', one that although has no visuality at the time (1960) it would have one from the 1980 edition (that of molecular models of the third-generation). **(see Figure 18, A and B,** see page 84 and 85 respectively**).**

As we learnt from the quantitative analysis **(Graph 1,** see page 114**)**, images of molecular models of third-generation emerged in the 1975 edition of CB. As we have seen in Chapter 1 molecular imagery had two previous manifestations, that of models of

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226 De Robertis, et al. 1960, op. cit., pp. 131-168 and pp. 456-494. The only exception is the mentioning of neurotransmitters such as acetylcholine during synapse.

227 Ibid. pp. 231-237.

228 Ibid. pp. 458-464.

the first-generation (paper formulae) and that of models of the second-generation, metabolic cycles, (3D models) of proteins and early molecular biology models **(Figures 18 A and 18 B,** see page 84 and 85 respectively**)**. Paper formula, and 3D models the associated imageries of the first (1900-1930) and second (1940-1970) waves of molecularisation in cytology, respectively both absent in Wilson's last edition (1925), began to manifest in the first edition of CB (1948) with images of molecules such as lipids, aminoacids and carbohydrates.[229] Key for the growth inside cytology of both types of images, especially 3D ones, as anticipated in Chapter 1, was the paradigmatic change that took place during the 23 years that elapsed between Wilson's last edition and De Robertis first one; that from colloidal chemistry to corpuscular 'molecular' chemistry. The use of molecular models of second-generation (3D models) was used more profusely in the successive editions of CB, as biochemistry became more and more a constitutive part of cytology (second wave of molecularisation), (see Chapter 1). The display of images of 3D molecular models in De Robertis et al textbook was quite original when compared with other contemporary textbooks, representing at the time, a significant crossing of disciplinary boundaries.[230] The 1960 edition displayed more sophisticated images alongside more nuanced textual information on proteins such as the structure of insulin as described by Frederick Sanger (1918- ) and the structural organisations of atoms in polypeptide chains including the β sheet and the α helix with its atomic rotations angles and so forth as developed by Pauling, Branson and Corey (see Chapter 1).[231]

229 De Robertis, et al. 1948, op. cit. Some examples: 3D models of molecules Fig 2, in pp. 20 (carbohydrates) and Fig 27, pp. 77 (polypeptide chain) and paper formula Fig 3, pp. 24 (lipids).

230 The first edition of De Robertis, et al textbook (1948) contained by far the largest treatment of the physicochemical components of the cell when compared to other contemporary cytology textbooks such as Gresson's, *Essentials of general cytology*, Gresson, 1948, op. cit. Whilst in De Robertis, et al treatise it was part of a full chapter with 30 pages (pp.11-41) De Robertis (1948), in Gresson it was part of a short chapter on the cytoplasm with only 4 pages, (pp. 10-14).

231 See De Robertis, et al. 1960, op. cit. Fig 2-1, pp. 19, in the Chapter 'Chemical and physicochemical organisation'. Insulin in figures 2-3 and 2-4, pp 20, polypeptide chains.

The other pictorial form belonging to molecular models of the second-generation that was widely used in biochemistry textbooks during the period between the 1930s and the 1960s is that of the complex cycle

s of intermediary metabolism such as the Krebs cycle **(Figures 18 A and 18 B, b,** see page 84 and 85 respectively**)**. It is remarkable that despite their wide use during that period, they were absent in the first two editions of De Robertis et al surveyed (1948, 1960). This situation changed in the fourth edition (1965) where images of metabolic cycles began to be displayed for the first time as part of a new chapter called 'Enzymes and cell metabolism'.[232] Metabolic cycles gained in complexity and were included in a different chapter from the 1975 edition 'Enzymes, bioenergetics and cell respiration' (pp. 58-77) a structure that will be kept in the further editions (1980 and 1987). Nonetheless, the visual landscape created by the microscopes and that created by biochemistry (as mentioned in chapter 1), were to remain noticeably separated. Images of the mitochondria and of the biochemical reactions occurring inside them (Krebs cycle and oxidative phosphorylation) for instance were located in different chapters of the 1980 edition of CB.[233]

The fourth edition of De Robertis et al (1965) is of particular relevance because it includes for the first time images of models of the second-generation other than those of biochemistry **(see Figure 18, B, d,** see page 85**).** It is in this edition of CB that the image of models from molecular biology such as the double helix model of DNA is shown for the first time in the textbook.[234] Other images belonging to this category in this edition are: a) the description of the Meselson and Stahl experiment designed to prove the semiconservative model of DNA replication, b) models of DNA replication in bacteria, c) model of protein synthesis and, d) the Jacob and Monod model (operon model) of control of the enzymatic induction of gene expression in bacteria.[235] The 1965 edition is also

232 De Robertis, et al. 1965, op. cit., pp. 41-53.

233 De Robertis, et al. op. cit., 1980. The image of mitochondria in chapter 12 'Mitochondria and oxidative phosphorylation', pp. 273 and the images of the cycles in Chapter 6, 'Enzymes bioenergetics and cell respiration', pp. 111.

234 De Robertis, et al. 1965, op. cit., pp. 30.

235 Ibid. pp. 301-303 and pp. 332, 335, respectively.

important because of the authors' first attempt to integrate in a single chapter the molecular models of the second-generation with the cellular phenomenon that those models were supposed to provide an explanation for. Thus, whereas in the previous edition (1960) a very simple version of the Meselson and Stahl model of DNA replication was, part of a chapter on the physicochemical components of the cell, in the 1965 edition the image of the model featured in the chapter that deals with cell division and that includes the condensation of chromatin into chromosomes and their subsequent displacements.[236] That said the molecular visuality remained again, as in the case of the images of intermediary metabolism, separated (in different chapters) from the classical cellular explanation of movements of chromosomes during cell division. The only exception is that of an image of a model proposing a mechanism for the spatial arrangement of the molecule of DNA during its replication into chromosomes as described by Taylor.[237] From this, it seems that the authors of CB were well aware of the difficulties of fruitfully combining cellular and molecular explanations.[238] It can be argued that uncertainty prevailed among the authors of CB concerning the extent that molecular visuality and explanation should have inside cytology.

Although it is not surprising that none of the images of molecular models used by De Robertis et al in their textbook were created by them, since they did not belong to that culture (see Chapter 5); this was also the case for many of the images of molecular models based on the images obtained with the authors preferred technology the electron microscope.[239] From the 1960 edition and with richer detail from the 1965 edition, images of molecular models based on the images obtained with the electron microscope are used to explain muscle contraction, as conceptualised by the at the time well-accepted

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236 De Robertis, et al. 1965, op. cit., pp. 291-320. Chapter 17 'Chemical and macromolecular organization of the chromosomes and nucleolus. DNA replication'.

237 Herbert J Taylor, *Molecular genetics*, Ed. J H Taylor, New York, Academic Press, 1963.

238 De Robertis, et al. 1965, op. cit., pp. 304.

239 These are Lynch's 'paired representations'. Michael Lynch, 'The externalized retina: Selection and mathematization in the visual documentation of objects in the life sciences', in M Lynch S Woolgar (eds), *Representation in scientific practice*, Cambridge, Massachusetts. London England The MIT press, 1990, pp. 153-186.

sliding filament theory.[240] The authors of CB, did not themselves produce the image of the model of muscle contraction, they just reproduced it with the permission of its author, who first created this paired representation of muscle fibers.[241] Another example of molecular models based on images obtained with the electron microscope that De Robertis et al imported into their textbook from other research groups is that of the lipid bi-layer model for the cell membrane originally proposed by Davson and Danielli in 1935 and further expanded by Singer and Nicholson in 1972.[242] The only exception to this was the images of models for synaptic transmission, which was the research subject of De Robertis himself.

It is worth emphasising then that in spite of the growing importance of molecular knowledge and visuality in cell biology, this was not a straightforward process for cell biologists of the traditional cytological school to undergo. Notwithstanding their willingness to engage with molecularisation, there were considerable hurdles to overcome first. It was not easy to integrate molecular explanation to back up many of the classic themes of cytology. By mainly focusing on the 1948, 1960 and 1965 editions of De Robertis et al textbook, our analysis so far suggests that microscopical imagery and with it microscopical culture led the field well into the 1970s just before the third wave of molecularisation began to extend its roots inside the discipline. All this, despite the attempts by De Robertis, Nowinski and Saez, three 'old guard' cytologists, to engage with the newly emergent molecular themes. A clear split was evident on what was cellular and what was molecular well until the mid 1970s in their treatise. A trend also observed in the vast majority of textbooks published at the time, such as Fawcett's *The*

240 De Robertis, et al. 1960, op. cit., pp. 502-505. De Robertis, et al. 1965, Chapter 21, 'Mechanical activity and cell motion', pp. 396-99. The sliding filament theory proposes that muscle movement, contraction and relaxation, is due to the displacement of filaments of actin and filaments of myosin (two proteins to be found exclusively in muscle).

241 The pictorial depiction of the theory is in fact a 'paired representation'. Hugh E Huxley, 'The double array of filaments in cross-striated muscle'. *Journal of Biophysical and Biochemical Cytology*, 1957: 3: 631-46.

242 De Robertis, et al. 1960, op. cit., pp. 121-127. De Robertis, et al. 1975, op. cit., pp. 154, Fig 8-6.
James F Danielli, Hugh Davson. A contribution to the theory of permeability of thin films. *Journal of Cell. and Comparative. Physiology*. 1935, 5: 495.
Jonathan S Singer, Garth Nicolson, The fluid mosaic model of the structure of cell membranes, *Science* 1972, 175: 720–31.

*cell* (1966, 1981), Kimball's *Cell Biology* (1970, 1978, 1984) and Dyson's *Cell biology a molecular approach* (1974, 1978).[243] From the mid 1970s a new wave of molecularisation, would enter cell biology and CB in particular, when the textbook incorporated a young molecular biologist as a new author. How did CB respond to this new wave of molecularisation? Would that entail a change at the level of its imagery?

### 2.3.2. The growth of the third wave of molecularisation in CB.

The 1975 edition of CB appeared when the third wave of molecularisation led by molecular biology, itself in constant transformation, began to grow inside the field of cell biology. Recombinant DNA technology emerged at the time and with it the possibility to translate the experiments on gene regulation as developed in prokaryotes, to eukaryotes (discussed in Chapter 5). Added to that, the new technology began to be increasingly used as standard practice in cell biology labs and hence to facilitate the achievement of those aims. The fifth edition of CB (1970) was the last one to be produced by the three original authors. The death of Nowinski, in 1975, forced the other two authors to look for a suitable successor. It soon resulted clear to them that Eduardo De Robertis (Eddie for short) the son of Eduardo Patricio Diego De Robertis was the ideal person to fulfil that role. Eddie De Robertis' 'molecular expertise' was expected to take CB into the new era cell biology was expected to undergo. He was a member of a new generation of scientists that started to use molecular approaches to the study of life, different to those used by the traditional cytologists.[244] Soon after his graduation as a medical doctor from the university of Uruguay in 1971 he began a PhD in chemistry at the Campomar Foundation and the University of Buenos Aires, a degree that he completed in 1974. His thesis was on the molecular control of bacterial growth by different metabolites, very much in line

243 Kimball, 1984., op cit. Robert Dyson, *Cell biology a molecular approach*, Boston London Sydney Toronto Allyn and Bacon, Inc, 1978. Another important book on cytology (microscopic anatomy) textbook for many years for students of medicine that first appeared is in Don W Fawcett, 1966., op cit. Fawcett textbook is based almost entirely on images obtained with the electron microscope.

244 From www.hhmi.ucla.edu/derobertis/doc/EDR_Website_CV.pdf (consulted in October 2008). One of the many young scientists that once formed in Europe or the US tried to bring those developments into their countries of origin.

with the operon model proposed by Jacob and Monod.[245] In 1975 he was awarded a Royal Society postdoctoral fellowship to work in Cambridge, England under the supervision of J B Gurdon a British scientist, pioneer on the use of molecular methods to study animal development.[246] In 1978 Eddie De Robertis moved permanently to England where he stayed until 1980 working as a member of scientific staff of the Medical Research Council Laboratory of Molecular Biology at Cambridge (LMB). The LMB at Cambridge was considered at the time (still nowadays) a dream location for a new molecular biologist to work at.[247] The institute was a well-recognised centre with a longstanding tradition in molecular biology and molecular genetics. The LMB hosted three Nobel prizes winners, Francis Crick, John Kendrew and Max Perutz. Inside it, some key findings hailed to be as major breakthroughs of the molecular culture took place. Among them: the unravelling of the structure of DNA (Crick) and proteins, myoglobin (Perutz) and haemoglobin (Kendrew) during the 1950s and 1960s, the development and production of monoclonal antibodies (Milstein and Kohler) and DNA sequencing (Sanger) during the 1970s.[248]

The LMB had a clear aura of being a privileged place where to learn about the 'burgeoning science of molecular biology',[249] especially for a young post-doc such as Eddie De Robertis who was willing to import that knowledge into eukaryotes, an area in which he had the opportunity to be one of the first specialists. As part of a new generation of scientists trained with the basic techniques of molecular biology such as DNA sequencing and cloning in the late 1970s, Eddie De Robertis was involved in an original

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245 Ibid. For details on the extension of the molecular paradigm from eukaryotes to prokaryotes see Chapter 3, subsection 3.1. '*Setting the scene'*.

246 Gurdon is credited for doing the primary work at the basis of what later was labeled as somatic cell nuclear transfer. In the 1960s he found that somatic cells retain the capacity of becoming embryonic again. By inserting the isolated nucleus of specialized cells in the cytoplasm of undifferentiated cells he showed that they were able to develop into any cell type. He also was one of the first scientists' to work on the identification and function of proteins produced in frog oocytes after injecting different messenger RNA, the work that Eddie De Robertis as a post-doc in his lab developed.

247 de Chadarevian, 2002, op. cit., pp. 2-4.

248 Ibid. pp. 9-12 and pp. 137-60.

249 Ibid.

piece of work at the time, that of the regulation of transcription of genes in eukaryotes, using frog oocytes as a model of a living cell system. By creating DNA constructions to expresses messenger RNAs he introduced those molecules into frog eggs (protein factories due to the huge amount of ribosomes they contain) and assessed not only their effect, but the biochemical properties of the different proteins produced. These were the kind of experiments that confirmed in everyday practice that the regulatory networks of genes found in prokaryotes by Jacob and Monod and others were also at play in higher organisms.[250] At the beginning of his postdoctoral years at the LMB in Cambridge in 1975 Eddie De Robertis became involved in the production of CB.

The inclusion of Eddie De Robertis, a molecular biologist, as a co-author had an immediate impact on the imagery of CB. As **Graph 1** shows in the 1975 edition, (see page 114), images of third-generation models feature for the first time in CB, albeit, in small number (representing a 1.52% of the total) and in a very schematic form, to explain the mechanism of hormone action, **(Figure 19,** see page 97**)**.[251]

From the epistemological point of view with regard to previous editions the one from 1975 expanded on molecular explanations for cell phenomena. The conjecture about the existence of membrane transporters, for instance, which first appeared in the 1960 edition,[252] to account for the phenomenon of internalisation of macromolecules inside cells was expanded and took a further molecular twist in this edition.[253]. The authors wrote:

> A possible molecular interpretation of the membrane pores is shown in Figure 21-3,C. The presence of embedded protein subunits is postulated within the lipoprotein structure. The pore could be envisioned as the interstice between four adjacent

250 See Chapters 1 and 3.

251 De Robertis, et al. 1975, op. cit., pp. 66, Fig 4-8.

252 De Robertis, et al. 1960, op. cit., pp. 231.

253 De Robertis, et al. 1975, op. cit., pp. 475-479.

protein subunits, which could form a hydrophilic channel across the membrane two such subunits are shown in Figure 21-3, C. [254]

At first sight this model for ionic transport including molecular pumps seems similar to the one developed by former physiological studies, which diagrammatically depicted molecular transport as simple arrows circularly traversing the membrane. This model belongs to a series of models based on those that were typically depicted in such journals as *Scientific American*, after the fluid mosaic model for the cell membrane originally developed by Singer and Nicolson in 1972.[255] In my view this kind of model belongs to a kind that preceded those presenting membrane embedded receptors (third-generation models). A closer look at it reveals that the pores are depicted as structures (embedded proteins) rather than just holes on the membrane, to explain the 'active' permeability of ions. Nevertheless, the depiction of these embedded proteins is very simple, even rudimentary specially when compared to the complex depictive standards that started to be featured in MBC. So, in the sixth edition of 1975 although a clear 'molecular' explanation is given for a cellular phenomenon the molecular imagery at least, one that arguably belongs to the third-generation just began to take form. This situation with slight variations would remain for the two editions that came later, that of 1980 and 1987.[256] Only in this last edition, that the image began to present a more defined form and depicted as showing the capacity of movement, a well-defined characteristic that the molecular models from the third-generation had. In the sixth edition of 1975 cell differentiation and cellular interaction was given a molecular explanation. This is perhaps not surprising as this topic was the first one to which molecular biologists such as Eddie De Robertis, were attracted to when they began working with eukaryotes.[257] Other topics of the textbook resisted molecularisation at the

254 Ibid. pp. 477.

255 Singer, et al. 1972, op. cit., pp. 720-31.

256 De Robertis, De Robertis, 1980, op. cit., pp. 154. Fig 8-17. De Robertis, De Robertis, 1987, op. cit., pp. 61. Fig 2-27. At difference of those in MBC, they were located in chapters of a molecular nature rather than cellular.

257 De Robertis, et al. 1975, op. cit., pp. 441-465, Chapter 20 "Cell differentiation and cellular interaction".

visual level. Amoeboid motion, for example, remained cytological until the 1975 edition and would remain as such, albeit, as part of a bigger chapter on cytoskeleton and cell motility well until the 1980 and 1987 editions. Two images from this edition (9-16 and 9-17) clearly show and explain in a pictorial manner the amoeboid movement as based on interactions between regions of different cytoplasmic density, instead of by molecules. From the quantitative point of view the total number of images of models of the third-generation increased from 0.57% in the 1975 edition to a 5.66% in the 1980 edition (published three years after the arrival of MBC) and stayed in that order (7.13%) in the eight edition of 1987 (published 4 years after the emergence of MBC). **(Graph 1,** see page 114**)**.

Some important conclusions could be arrived at from our discussion of the imagery contained in all the editions of the De Robertis et al textbook. Firstly, it is clear that at the structural and organisational level most of CB editions (until the 1970s) would conform to the general plan set in the latest edition (1925) of Wilson's textbook. It will have, as many others books on cells, one main theme, that of 'structural cytology' and two others, namely: genetics and biochemistry, all of which acted as conceptual organisers for the arrangement of chapters.[258] Secondly, despite the growth of the different visual forms of molecular culture, microscopical images remained dominant throughout all editions of CB. Thirdly, despite this growth, microscopical and molecular imageries remained separated. This can be illustrated by the fact that well until the mid 1970s the depictions of the molecular reactions occurring inside organelles remained in different chapters than those dealing with the organelles themselves. Mitochondria, for instance, have their own chapters in the editions of 1948, 1960, 1965, and the 1975 edition. The biochemical reactions occurring inside them, such as the Krebs cycle and the respiratory chain, although discussed in those chapters, have a very succinct treatment.[259] In other cellular processes microscopical and molecular imageries also remained

258 A couple of exceptions from all textbooks surveyed by the author are those of: C E Walker, *The essentials of cytology*, London, Archibald Constable & Co. LTD, 1907. This book only contains a few drawings of cells and do not engage at all with biochemical or genetic issues, and Lester W Sharp. 1906, op. cit., a textbook that does not include the biochemistry of cells.

259 De Robertis, et al. 1975, op. cit., pp. 58-77, Chapter 4 'Enzymes bioenergetics and cell respiration' and pp. 200-30, Chapter 10 'Mitochondria'.

separated without any overlapping. Themes such as the endoplasmic reticulum and protein segregation (the separation of proteins from the membranes of the endoplasmic reticulum after synthesis) were 'visually unconnected' in the successive editions of CB until that of 1975. They began to coalesce only in the 1980 edition when chapters on the endoplasmic reticulum began to show visual forms such as the synthesis of proteins by ribosomes associated to the membranes of the endoplasmic reticulum.[260] Although this trend showed some signs of reversal when Eddie de Robertis, a member of the new molecular culture joined the production of CB from the 1975 edition onwards, microscopical visuality would remain dominant in that edition until that of 1987. So, visually and epistemologically the claimed analysis of sub-microscopic organisation was still predominately about making connections with knowledge claims at the structural level and taking the cell as a whole. In other words the 'cellular model' was a key epistemic theme for CB. The theme of neurobiology, a speciality of Eduardo De Robertis, is a good example to illustrate more specifically this point on the centrality of the cellular model. Only one model is featured in Chapter 22 'Cellular basis of nerve conduction and synaptic transmission' of the fourth edition of 1965, to explain the behaviour of nerve cells (with cell parts such as vesicles forming and discharging their contents). In the equivalent chapter, number 28, 'Cellular and Molecular neurobiology' of the 7th edition of 1980, six models of this nature are depicted.[261]

Lastly, there are no doubts that the inclusion of Eddie de Robertis, a molecular biologist, to CB has an immediate impact for the appearance of molecular' imagery of third-generation in the textbook. Nonetheless, chapters in all the editions he participated (1975, 1980, 1987) were written from either a cytological or a molecular standpoint. All the chapters dealing with molecular themes such as those including DNA duplication and protein synthesis were written by Eddie de Robertis. The only exception to this is the area of synaptic transmission, an area in which Eduardo De Robertis was an active participant by finding the role (among other groups) of the enzyme adenylate cyclase as a 'second

260 Images that are considered to contain molecular models of the third-generation because of the association of molecular processes with sub-cellular structures involved in a cellular activity such as secretion. De Robertis, et al. 1980, op cit., pp. 213, Fig 10-7 pp. 222, Fig. 10-12 and pp. 223 Fig 10-14.
261 Although many of these images are interpretations of electromicrographs, the overriding theme is about cellular function.

messanger after the interaction in the target cell of the neuroransmitter dopamine with its receptor. That said, in the 1980 and 1987 editions of CB molecular imagery was displayed by and large in molecular chapters rather than in cellular ones. The use of the conjunction 'and' between cellular and molecular in the title (*Cell and molecular biology*) is, in my view another expression of this disengagement. Its use symbolises an attempt to denote the existence of two different epistemic realms as represented by the De Robertis father and son both belonging to different epistemic cultures, the microscopical and the molecular respectively.

### 2.4. A brief overview of the epistemic landscape of cell biology before the publication of MBC.

Our previous discussion gave us an idea of the key epistemic problems cell biology was addressing in the hands of former cell biologists just before MBC appeared. We have seen that despite CB increasingly moving towards molecularisation from the 1970s, microscopical visuality was dominant and cytological themes were by and large disengaged from the molecular themes as developed by molecular biologists (gene regulation, protein synthesis etc). A complementary way of getting an insight into the key epistemic problems cell biology faced before the emergence of MBC is to track down the views on this issue of the main figures of the transformation of cytology in cell biology during the 1940s to 1970s (see Chapter 1). To put it into a question form: Were the 'old guard' cell biologists contemplating a full-scale molecularisation for their discipline? If that was the case, what sort of molecularisation was that one to be?

Some clues to this issue are found in the concluding remarks for the first international congress of cell biology that took place in Boston USA in September 1976.[262] Palade (a key player for the transformation of ctology into cell biology)[263] identified there some 'unresolved issues'; he mainly referred to that of intracellular

262 B R Brinkley, Keith R Porter (eds), 1976-1977, Papers presented at the First International Congress on Cell Biology, Boston, Massachusetts. (The Rockefeller University Press In Cooperation with the American Society for Cell Biology and The Journal of Cell Biology) pp. x. Palade described himself as an 'old guard' cell biologist to differentiate himself and his colleagues from the molecular biologists that began to enter the discipline in the late 1970s.

263 See Chapter 1, subsection 1.1.2 *'The expansion of microscopical imagery: The electron microscope'*.

protein transport'.[264] Research on protein production, transport and in particular their processing (the inclusion of sugar groups) and final secretion through the membranes of the rough endoplasmic reticulum were in Palade's view the kind of research topics cell biologists should be pursuing at the time. The 'signal hypothesis' was another theme that concerned Palade, one that if resolved, as he argued, would take cell biology into another dimension.[265] The hypothesis refers to the existence in a growing polypeptide of a signal that helped the targeting of the polysomes (a group of ribosomes) into the membranes of the Rough Endoplasmic Reticulum, a structure responsible for the extracellular export of secreted proteins. Still another issue that Palade saw as relevant was that of the transport of proteins in the Golgi complex and the role of the interactions between membranes inside the cell during the secretory pathway. All in all a cellular theme, that of the study of intracellular protein secretion was high on the agenda for one of the 'creators' of modern cell biology.

Although the themes that Palade identified as hot spots to be studied were in essence cellular ones, the resultant imagery was of a hybrid nature. In effect the new imagery of protein transport and secretion although containing elements of the second-generation of molecular models (ribosomes translating a messenger RNA into a protein), they included cell organelles and processes such as the transformation of membranes of the rough endoplasmic reticulum into those of the Golgi apparatus through vesicles for the externalisation of cellular membrane embedded proteins.[266]

Overall however, Palade was asking for solutions that his generation, as we saw before in the case of De Robertis et al, could by and large no longer offer. The views and practices of Palade's generation were somehow limited and unable to incorporate fully

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264 George E Palade, 'Greetings to the congress' in Brinkley, et al. 1976-1977, op. cit., pp. 337.

265 Brinkley, et al. 1976-1977, op. cit.

266 It is because of this hybrid nature and its connections to cell structure and cell function that this imagery (processing an maturation of proteins) is considered here alongside to that on signal transduction and receptors with signal functions or membrane transporters, as the 3rd generation models of molecular culture.

the new molecular knowledge and its associated practices.[267] Palade was quite explicit in this regard when he greeted the participants of the first international congress of cell biology in 1976, he stated:

> Like the old kingdom of Spain, we have lost to some enterprising late-comers, quite a number attractive provinces on which our standards were originally planted. The mitochondria have been virtually annexed by the biochemists, and the ribosomes have been taken over almost entirely by molecular biologists […] We should also realise that the period of discovery and initial exploration in cell biology is practically over, and that the old idea of integrating structure, biochemistry and function for each subcellular component considered in isolation, through still valid, is no longer sufficient. The interest is already shifting toward regulatory mechanisms. [268]

To which he later in his speech added:

> The time of a major change of the guard is rapidly approaching. Perhaps this is the last time when the old guard--that medley of hard-working pioneers, wise founders, and demanding bosses-will parade in strength.[269]

Needless to say, it did not take that long for Palade's predictions to come true. From the subject matter of the papers presented at the second international meeting in cell biology held in Berlin in 1980 it is evident that things began to change in cell biology.[270] Not only that, new techniques and reagents such as monoclonal antibodies, began to be extensively used in different areas other than the purification of fractions, such as the identification of the different cell populations in cancers for instance, but that the new practices of molecular biology and their associated buzzwords such as 'gene mapping'

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267 With the exception of monoclonal antibodies. Palade viewed them as key agents to get rid of the molecular contamination that threatened the success of the molecular experiments in cellular transport. B R Brinkley, Keith R Porter (eds), 1976-1977, op. cit. (Palade Preliminary remarks). The contamination refers to the presence of molecules from a different organelle from the supernatant getting absorbed to a fraction that it did not belonged to.

268 Brinkley, et al. 1976-1977, op. cit., pp. viii-ix.

269 Ibid. pp. x.

270 H G Schweiger, (ed) 1981, *International cell biology 1980-1981*. Papers Presented at the Second International Congress on Cell Biology Berlin (West) August 31-September 5, 1980, Berlin, Heidelberg New York, Springer-Verlag.

began to be used with an increasing frequency in the field. Cell biology was ready for a generational renewal with the last remnants of the old microscopical tradition ready to concede their epistemic and visual domination, the one that Wilson established at the beginning of the 20th century by putting the cell at centre stage.

The full-scale transformation of cell biology, the 'change of guard' that Palade predicted, did not originate from the inside. It came chiefly from a new group of determined molecular biologists that were to some extent foreign to the discipline. Key among a group of non-cell biologists, were those who found irresesistable the enormous enthusiasm of James Watson for molecularising cell biology by (among other initiatives), writing a textbook on it. That MBC, one of the most successful books in cell biology, was written by a group of non-specialists is also confirmed by the fact that none of the scientists who finally become authors of it presented papers or even participated at neither the first (Boston, 1976) nor the second (Berlin, 1980) international meetings in cell biology.

The next chapter describes many of the inner workings of the production of MBC and with it key aspects of the conformation of the visual change in cell biology.

## Chapter 3. The making of Molecular Biology of the Cell.[271]

### 3.1. Setting the scene.

MBC was part of the first steps of a wider initiative that Watson felt both inevitable and necessary, that of refashioning the whole of biology by giving it a comprehensive molecular outlook.[272]

One key element for the expansion of this molecular outlook that would become dominant was to establish mechanisms that interconnected without any fissures two key places for the production of knowledge: the place where experiments and knowledge are produced, the laboratory, and the place where newcomer students are formed, universities.[273] Since the mid 1970s many laboratories began to adopt the programs and practices of molecularisation (cloning genes and analysing expression patterns), the work that remained to be done to ensure its constant reproduction would be carried out within education programs at universities. Essential for those programs was the creation of new textbooks allowing the opening of new forms of visual and epistemic expressions aiming to displace the previous microscopical outlook given to the discipline by textbooks such as CB (see Chapter 2) and thus allow for the expansion of the paradigm of molecularisation.

A textbook that was playing an important role during the first period of the molecularisation of biology (from the late 1970s) was James Watson's *Molecular Biology of the Gene* (MBG). MBG was the first publishing venture for Watson and as

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271 This chapter is based on the interviews conducted by the author with three of the authors of MBC Martin Raff, Julian Lewis and Keith Roberts. MRI 00 10. 05 means Martin Raff Interview zero hours, ten min, and five seconds as registered in a MP3 file. For more details on how the interviews were performed see Appendix, subsection A.4. *'Interviews'*.

272 See Chapter 5, subsection 5.1.3.*'James Watson: Building the scientific self of molecularisation: The Harvard years (1956-1976) and beyond'*. Watson vision of molecularising biology as a whole is well documented in John R Inglis. Joseph Sambrook and Jan A Witkowski, (eds) *Inspiring science: Jim Watson and the age of DNA,* Cold Spring Harbor, New York*,* Cold Spring Harbor Laboratory, 2003. This book was written in his honour by people who had interacted with him. Particularly revealing for his vision on molecularising biology is Watson's confrontation while in Harvard with Edward Wilson a paleontologist (pp. 206 and pp. 183-187). Also it is important to flesh out Watson ideas for molecularising biology is his role as director of Cold Spring Harbour (see pp. 227-361) and from his role in the Asilomar conference and the Human genome project pp. 365-412.

273 This regardless of their locations (if they existed or not in the same building). Many laboratories are not associated to universities. The interconnection of objectives is what it mattered most.

such the book that in many respects set the tone for the production of MBC.[274] In it the following principles for textbook writing that were much cherished by Watson were applied: a) to be the first to tell a good story, b) to use snappy sentences to open your chapters c) to challenge your students to move beyond facts. These were all maxims that were applied during the writing of the first edition of MBC (1983), and even perfected in during the writing of its successive editions (1989, 1994, 2002 and 2008).[275]

MBG was considered by its editors to belong to a series of textbooks aimed to help biology teachers in the design of new programs for undergraduates in a biology that was at the time going through deep transformations.[276] MBG was one if not the first specialised textbook acting as a vehicle for the perpetuation and expansion of the molecular paradigm inside biology written for a wide audience, students of different levels as well as senior investigators. As Paul Doty put it, once 'the molecular biology revolution was in full force: It needed a tribune'.[277] MBG was the perfect textbook for that tribune, for it was at that point in time (1965) that it presented all the major findings of the classical period of molecular genetics (1940s-1960s) that any student needed to know in order to become a molecular biologist.[278]

With molecularisation practices running in many laboratories around the world, at the level of textbooks a little snag remained, one that if not acted upon could threaten Watson and others', longstanding wished expansion of the molecularisation programme. MBG, however successful, remained a molecular genetics textbook. The majority of the molecular processes described in it were not related to the cellular process occurring in

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274 James D Watson , *Molecular biology of the gene,* New York, W A Benjamin Inc, 1965.

275 James D Watson, *Avoiding boring people and other lessons from a life in science,* Oxford, Oxford University Press, 2007, pp. 236-7 and pp. 133 respectively.

276 Watson, 1965, op. cit., pp. vii, (editors foreword).

277 Paul Doty 'Watson at Harvard (1956- 1976)', in J Inglis, J Sambrook, J Witkowski, (eds), *Inspiring science: Jim Watson and the age of DNA.* Cold Spring Harbour, New York, Cold Spring Harbor Laboratory, 2003, pp 203-9, on p. 206.

278 As shown in the previous chapter CB also featured them but in simple and succinct way when compared to MBG.

eukaryotic cells, which were by and large not the subject of MBG. They only have a little space in the first chapter 'The Mendelian View of the World' where the Mendel laws are introduced, in the chapter where the problems of cell differentiation and antibody synthesis are introduced by using as example eukaryotic cells from organisms like drosophila and rabbits respectively. And also in Chapter 16 on cancer, where eukaryotic cells are mentioned but always with a reference to viruses, which were considered at the time as the most important causative agents of the disease.[279] Although true that from the third edition of 1976 MBG incorporated more themes of eukaryotic biology, as a whole the eukaryotic cell remained an uncharted territory in it, a condition that seriously distressed Watson.

In trying to keep abreast of the changes occurring in the labs where increasingly genetic engineering based experiments with eukaryotic cells were taking place, Watson took the decision to produce MBC and with it the third-wave of molecularisation of cell biology was set in motion.

### 3.2. The making of MBC.

The first piece of evidence of the intention to write MBC I found is from a letter from Jim Watson to Keith Roberts dated the 2nd of July 1974.[280] In that letter Watson invited Roberts to visit CSH in the USA with the aim to revise the illustrations he made for the, at the time, the forthcoming 3rd edition of the MBG. In the P.S of that letter Watson wrote:

> Would you be interested in being one the authors of a cell biology text. Bob Goldman (microfilaments) and Bob Pollack have talked here about one and if you would join them, I suspect the final product could sweep the field.[281]

279 Watson, 1965, op. cit., pp. 2-31.

280 Letter from Jim Watson to Keith Roberts dating, July 2, 1974. Keith Roberts provide the author with a copy of it.

281 Ibid.

Watson took the making of a new book on eukaryotic cells as a very serious affair, one that would have, if accomplished, long-term consequences for the discipline, one that 'will sweep the field' as he remarked in that letter he wrote to Roberts in 1974. Watson was so convinced in the production of a book on cells from a molecular perspective that in trying to convince Bruce Alberts to become an author in the early 1978, Watson told him:

> Bruce the point is that no matter what you or Martin or Keith or me or anybody else does in science somebody else is going to do it in weeks in months at worse in a couple of years, but this book, if you guys don't do this book, none is going to do the book this way and a whole generation of cell biologists will be deprived, so this will be, if you take it on and do it well, it will be the most important thing you do probably in your careers.[282]

For Alberts, who just at that time was appointed as a Professor at the University of California in San Francisco's medical school, this was a bold offer and represented a big challenge, but one that due to his expertise on the molecular basis of protein complexes during chromosome replication, he felt willing and able to pursue.

Watson was never really bothered with the fact that none of the authors he began to gather were cell biologists or that he was not a very committed writer. In fact he was quite outspoken about it. In one of the inaugural meetings to discuss the organisation and incorporation of new authors for the writing of MBC, he told those present: 'we need to have a real cell biologist, none of you guys is a real cell biologist'.[283] Watson himself was also not a cell biologist and for Raff 'it was clear he wasn't going to be the best writer either.[284] Raff stated that, Watson 'never wrote much', (and that) 'even in the first edition there may be five or six pages of his writing on viruses'.[285] A case that confirms

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282 MRI 00.08.54. Martin and Keith refers to martin Raff and Keith Roberts respectively, see later on here on Martin Raff and subsection 3.2.6 on Keith Roberts.

283 MRI 00.11.56.

284 MRI 00.21.12.

285 MRI 00.45.38.

his role as that of an initiator/motivator, but ready to leave the job once on his view, it became monotonous and dull.[286] In the end writing a textbook on a new subject like cell biology was a thrilling experience for everyone, an experience that brought a sense of personal fulfilment, new friendships and above all, despite the hard work, a lot of fun. Julian Lewis for instance, stated that 'It was fun working on the first edition, It was exciting because none of us of us knew any cell biology so it was fun to feel that we were doing something new'.[287] The previous statements that Watson and Lewis made only confirms the sense of a challenge and risky adventure that the molecularisation entailed for the new kind of entrepreneurial scientific selves (see Chapter 5). Unexpectedly and in part as the result of being written by non-specialists, MBC rather than being a molecular approach to different kinds of organisms as it was originally planned to be,[288] resulted in a book that gave a molecular explanation to classical cellular themes such as cell movement or cytoskeleton structure. As such, MBC began to function as the embodiment and a hallmark of the molecularisation in cell biology. MBC began to some extent to overwrite Wilson's message of taking the cell as key organiser of biological functions, and conceptualise the cell instead, as Alberts stated, as 'half-way between molecules and man'.[289] By doing this MBC would also become both a comprehensive map with instructions on what to do with cells and a magnifier with which to look at them and at the whole of biology.

No doubt Watson would do anything he could for the textbook to be a success even if was to be written by non-specialists. However, he wanted more authors. The process of gathering authors for MBC continued, so by the beginning of 1976, James Watson instructed a publisher (one that resulted not to be the final publisher of MBC) to phone Martin Raff from University College London (UCL) to let him know that he was interested in doing a book in cell biology and ask him if he would be interested in

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286 He is credited as expressing in 1989 soon after the crusade for the sequencing of the human genome began that 'after a year or two, the job will become just one of micromanagement, and I'm not interested in that, so I'll leave' (Quoted in Victor K, McElheny, *Watson and DNA: Making a scientific revolution*, London, John Wiley& Sons Ltd, 2003, pp. 263.

287 JLI 00.03.05.

288 KRI 00.03.15.

289 Alberts, et al. 1983, op. cit., pp. 3.

becoming involved. Martin Raff, who originally had trained as a medical doctor, more precisely as a neurologist, soon became unconvinced of his own capabilities as a practitioner and decided to become an investigator on the biosciences. Soon after his career change Raff saw his career boosted. He began to be seen as a specialist in the field of cellular immunology some years later after he published in 1969 an important paper in the journal *Nature* about the description of a specific marker for lymphocytes, a cherished result for the community of immunologists looking for the holy grail of molecular markers for cellular specificity.[290] Raff's prominence did not escape Watson's attention, which was focused on finding bold writers for his new book.

Following Watson's instructions the publisher invited Raff for an informal meeting to take place in London six months later to discuss the issue.[291] Although rejecting the invitation at first on the basis that he just had an awful experience of writing a book on T and B lymphocytes that nobody read, Raff, after some insistence from the publisher, finally agreed to meet the incipient group.[292] It was at that meeting that Raff changed his mind and decided to become an author. On that occasion another important change occurred, a new publisher named Gavin Borden was in the process of replacing the first. At that meeting in London were present three of the final authors of MBC (Watson, Raff and Roberts). The other two final authors Dennis Bray, a cancer specialist working at Kings College in London and Julian Lewis a main investigator in the development unit of the Imperial Cancer Research Foundation also from London, would join them later **(Figure 25)**. Bray joined the preliminary discussion group at the following meeting and was asked to write about the cell cytoskeleton. The first draft he sent some time later was enough to convince Watson, Alberts, Roberts and Raff that he deserved to be an author. Lewis joined even later when the 'team' was already gathering together to design the book final layout.[293] His involvement somehow began when he met Alberts

290 Martin Raff. Theta isoantigen as a marker of thymus-derived lymphocytes in mice. *Nature*, 1969, 224: 378-79.

291 MRI 00.43.00.

292 MRI 00.46.00.

293 JLI 00.00.40.

**Figure 25: The MBC 'team' at Fort Hill, 1982. From left to right Bruce Alberts. Keith Roberts, Martin Raff,Kevin Borden, James Watson, Dennis Bray, Julian Lewis. (Picture courtesy of Keith Roberts)**

who spent a sabbatical in London and shared a room with Cheryl Tickle a developmental biologist colleague of Lewis. Tickle got first invited by Alberts to write that chapter on developmental biology for MBC, but decided to join forces with Lewis because it was otherwise too much for her (she later abandoned the initiative).[294] Lewis took the first draft to CSH where all the others were working and presented it to a meeting there.[295] Lewis joined Watson, Alberts, Raff and Roberts at perhaps one of the lowest moments of the group, a moment during which after two years of some gatherings together the general feeling was that they had lost the plot.[296] Lewis turned up when they were evaluating the writing done by a list of 'experts' that Watson, Alberts, Raff and Roberts had selected in a previous meeting to potentially consider them as authors. Lewis remembers the feeling that things seemed to be going nowhere. The first chapter drafts that came in were in Raff's view 'not even close to be a potential chapter'.[297] They were enormously long and some very detailed, some tiny, some very inaccurate; they did not fit together at all.[298] After the authors read Lewis' chapter on development, they liked it so much that he was invited to join the 'team' as a co-author.[299] In Raff's recollection of events Lewis's incorporation was just the right thing occurring at the right time. In his own words: 'this immediately became our best chapter and it was such a boost that we needed desperately, and if that didn't happen I am not sure this book would have happened, it was really fundamental'.[300]

So by the time Lewis joined all things began to change, as we will see shortly, when they began to gather together for longer periods of time to write the chapters by themselves. The idea of creating a team of writers gathering together in isolated places

294 JLI 00.00.53.

295 JLI 00.01.35.

296 JLI 00. 02.12.

297 MRI 00.27.38.

298 JLI 00.03.30.

299 MRI 00.28.25.

300 MRI 00.28.28.

was an initiative of Watson and the new publisher Gavin Borden, this last, a central figure for the production of the book.

### 3.2.1. A key work for an inexperienced editor: The work of Gavin Borden in building the MBC 'family team'.

In Martin Raff own words Gavin Borden 'turned out to be the perfect publisher for us'.[301] Borden was a former linguist and classicist from Harvard where he met Watson and they remained very close friends.[302] Without Borden's predisposition and especially without his charisma, his entrepreneurial and adventurous character, Watson's idea to write a book on the molecular biology of eukaryotic cells would never have taken place. All the authors praised his determinant role for the production of the book.[303] They openly acknowledged his input in the preface of the first (1983), second (1989) and third (1994) editions (he died three years before the third edition got published) with words describing his demeanour and general manner of work producing feelings of: 'generosity', 'hospitality', 'friendship', 'kindness', 'good humour', and 'efficiency'.[304]

The production of the book was a real risk especially for a new and not well-known publisher such as Borden. He and his wife Libby, before getting involved with MBC, ran a small family publishing company (Garland Press) that was mainly involved in 'small jobs' such as the reprint of theses for universities (expensive facsimile editions for academic libraries).[305] The two most significant productions Borden and Libby had been involved before was that of a small art book and that of a facsimile of James Joyce's holograph manuscripts for Ulysses.[306] Therefore, producing MBC was a huge task to undertake for Borden, for in addition he had no experience at all in the field of scientific

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301 MRI 00.39.35.

302 KRI 00.09.50.

303 JLI 00.04.30.

304 Alberts, et al. 1983, 1989, 1994. (Prefaces).

305 MRI 00.14.00.

306 KRI 00.09.28.

publishing. Moreover, his company was almost at the verge of economic bankruptcy.[307] In Keith Roberts' view 'he was running into quite a 'severe low cash problem by the time the book came out'.[308] Despite the risks, Borden 'was persuaded by Jim (Watson) to do this sort of 'manic thing' that allowed him to have this sort of 'blind faith in the project', commented Keith Roberts.[309] This kind of positive attitude Borden took and transmitted to the authors was essential for the production of MBC.

Borden was not only adventurous but also very entrepreneurial, charismatic, well organised and above all a highly trustable person, so, he took all the precautions and necessary steps required to take when confronting this new business opportunity that MBC represented. In line with market research strategies developed by business companies to warrant a successful sale in business, he embarked on such a prodigious adventure with an attitude of solid entrepreneurialism and self-confidence.[310] In fact, Watson's conviction that 'this could be a significant sell because there was a real niche' in the market to exploit, was based on that extensive market research conducted by Borden.[311] Basically, Borden's market research exercise showed that, on the one hand, there were an increasing number of courses getting out-of-touch with the science being practiced in the labs (something that Watson suspected from his own experience at Harvard.[312] In effect, in most US universities courses were lagging behind the 'new biology, they were too 'structural' (based on microscopy). In addition to this, textbooks on the area out of touch with those developments and consequently they were not serving the integrative function a textbook required for the molecularisation of cell biology should deliver.[313] De Robertis et al CB was considered to be too 'structural' and another one by Haggis et al *Introduction to molecular biology,* too 'molecular'.[314]

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307 MRI 00.14.00. This was the overall view of all authors interviewed.

308 KRI 00.08.30.

309 KRI 00.09.50.

310 For the social background in which people like Borden developed his 'virtues', see Chapter 6.

311 MRI 00.04.50.

312 See chapter 5 subsection 5.1.2 *'James Watson: Building the scientific self of molecularisation: The Harvard years (1956-1976) and beyond.'*

313 MRI 00.05.00.

In the end Borden managed to gather 1 million US dollars to pay for the initiative to proceed. That money paid not only for the market research, but also for all the authors personal expenses including the rents for the places they stayed in when they gathered together, as well as the travel to the different venues where those gatherings took place, (Paris, London New York, San Francisco).[315] In effect, countless regular meetings in London followed that first meeting at Fort Hill, for which Borden even bought an old book-store house in London at St John's Wood near Abbey Road studios where Keith Roberts and Julian Lewis lived on and off for several years.

The importance of Gavin Borden for the production of MBC goes well beyond, the market research he had carried out and the money he invested for its production, which included the authors' personal expenses, and the renting of venues to get the textbook underway (he continued to do that job on the further editions). Borden had an essential role in creating the right conditions to build the 'family-team spirit' that he was convinced the authors would need to write as freely and as creatively as possible, a feature in the production of MBC that made it distinctive. Borden's approach of 'working hard and having fun' suited and was similar to Watson's ambitious, playful and competitive style.[316] Watson derived this style from his former boss Salvador Luria, who together with Max Delbruck, both the founders of the 'phage group', adopted as a way of practising research during the 1940s and 1950s. This style, 'with its apparent absence of hierarchies, freedom of discussion, and a close mixture of work and pleasure', could be traced back to Niels Bohr's own working style in physics.[317] In fact it was from him that Luria and Delbruck learned it and decided to apply it as a working practice for their phage group.

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314 Haggis, et al. 1964, op. cit. Borden and the rest of the authors considered that these books failed to integrate morphological cell biology with the 'new' molecular cell biology. (MRI 00.05.00).

315 KRI 00.09.00.

316 Shapin, 2008, op. cit., pp. 217-8.

317 Morange, 1998, op. cit., pp. 46.

Having fun and working hard was the distinctive working atmosphere that Borden constantly encouraged and that all the authors enjoyed. It was Borden's achievement to make of a so dissimilar group of writers a 'family'. This atmosphere facilitated by Borden is remembered with special fondeness by Keith Roberts who commented:

> […] So crucial and valuable for the book is that the particular mixture of authors we ended up with, was one …all of us having enormous respect for each of the others but perfectly happy to be critical of, you know, friendly critics of the work, so the idea of being a communal, co-produced text or co-generated text with each had specific areas of expertise […] from where to refer to, but each having an input into everything, it was a very delicate balance and that sort of willingness to pull together be part of a team […] Julian and I shared a room, in the…a bedroom, in a house at Saint Jhon's Wood, […] we have sleeping in the same room for well over a year total time […] which is quite a long time, you know, you really get to know people throughout that sort of interaction and so on, it was…it was terrific.[318]

Julian Lewis also remembers Borden with a smile in his face, he stated concerning him: 'We were very generously supported by Gavin Borden the publisher […], he is an interesting character, but anyway he made it fun for us, and so it was quite exciting ……we stayed at his house for a while at his flat in New York'.[319] Borden was also very sensitive towards the authors' likes and dislikes. Roberts remembers the occasion when Borden offered to him a copy of a classical work by Le Corbusier, one of his favourites architects, containing facsimiles of all his architectural drawings for that work.[320] Borden with an enormous diligence and effectiveness constantly made sure that everything was always in place, as Raff put it, working with Borden, 'you always had the feeling that whatever you needed you could have […] if we needed another expert to

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318 KRI 00.10.20.

319 JLI 00.04.35.

320 Keith Roberts, 'On drawing molecules', in J Inglis, J Sambrook Jan Witkowski (eds), *Inspiring science: Jim Watson and the age of DNA*, Cold Spring Harbor, New York, Cold Spring Harbor laboratory Press, 2003, pp. 437.

write something he 'd never say no, it would be too costly'.[321] In addition, Borden never put pressure on the authors to produce the book, in Raff 's own words:

> In fact he was the opposite, so when we were in these group meetings he would drag us away to play tennis, he would drag us away to go swimming or boating or something, you know… he made it like a summer camp to make it fun, […] fundamental, absolutely fundamental. [322]

### 3.2.2. Some other key figures: Miranda Robertson as the perfect companion for Borden, Keith Porter and the 'culture clash'.

Six weeks after that first meeting in London a very informal one followed at Watson's house in Martha's' Vineyard a summer destination north east of Manhattan on the east coast of the US, in early 1977.[323] No serious conclusions were reached at that meeting except to meet again later in the year following James Watson's insistence on the necessity to finally get the book underway. They met again more formally a few months later in a mansion at Fort Hill, close to CSH also on the East coast of the US **(Figure 26)**. Among the participants at that meeting at Fort Hill were Gavin Borden and all those that would later become the core writers of MBC: Jim Watson, Martin Raff, Bruce Alberts and Keith Roberts.[324] At that meeting, which lasted six weeks in total were also, two interesting personalities Miranda Robertson, who later would become a key person for the publishing of MBC and the well-known cell biologist Keith Porter.[325]

Miranda Robertson, was a former editor of *Nature*, and began to work as the developmental editor for MBC in 1976. She was acknowledged in the preface of the first edition of 1983 as playing a pivotal role in the writing of the chapters by insisting on the

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321 MRI 00.39.50.

322 MRI 00.40.52.

323 None of the authors interviewed remembers the exact date when that meeting took place.

324 MRI 00.02.18.

325 KRI 00.06.45.

**Figure 26: Discussing the making of MBC at Fort Hill. 1982. From left to right: Martin Raff, James Watson, Bruce Alberts, Keith Roberts, Gavin Borden, Keith Porter, Miranda Robertson. (Picture courtesy of Keith Roberts)**

fact that every page has to be 'lucid and coherent'.[326] She together with Borden did something of a novelty at the time for the context of academic textbook production by bringing together a massive feedback of opinions and opportune suggestions from university undergraduate and graduate students, university teachers and outside experts. Robertson did all this work also for the second (1989) and the third edition (1994) of MBC, to keep the book always attuned to the students' needs. The reports gathered by Robertson were carefully read by the authors and helped them to improve the quality of the content of the textbook by positioning them as close as possible to the interests of their potential consumers. In other words Robertson made of a MBC a constantly 'consumer tailored product'

As anticipated the other key personality present at the meeting in Martha's' Vineyard was Keith Porter, a well-regarded member of the 'old guard' of cell biologists and hence, in Watson's appreciation, the only 'proper cell biologist' at that meeting. Despite belonging to a different generation and as such not seeing under exactly the same perspective the 'new' problems cell biology confronted for the others, he was nevertheless invited by Watson to participate. Keith Porter was the oldest author, he was in his late 60s, all the others, with the exception of Watson who was 50 were roughly in their early 40s. The possibility of Porter becoming one of the authors of MBC was soon perceived as troublesome by Bruce Alberts and Martin Raff who did not like him on the grounds that Porter was an 'old guard' guy, a too morphologically oriented cell biologist.[327] Watson's argument for Porter to become an author of MBC was that Porter was 'Mr cell biology in America', and that he had the best electron microscopy pictures of cells, not only 'in town', but, 'on earth'.[328] Watson's arguments to incorporate Porter as an author eventually sounded convincing to both, assuring the entry of molecularisation into traditional cytology and warranting a significant sale for MBC.

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326 Alberts, et al. 1983, op. cit., pp. xi-xii. Miranda Robertson would be acknowledged for her role until the third edition of 1994. She left Garland publishing in 1998 to work for another publishing company (From Keith Roberts to the author. March 2010).

327 MRI 00.23.15.

328 Ibid.

One day in 1978, Porter went to one of the first working meetings at Fort Hill and presented the beginning of a chapter presumably on the cytoskeleton, a chapter that it turned out had been written by one of his post-docs in the lab. This was perceived as a hindrance by the rest of the authors. In fact, more than that, that event was to be the 'drop that overflowed the vase' for Alberts and Raff who always looked at Porter with suspicion. In Raff words when describing that event 'he was abysmal' (Raff meant appalling, dreadful).[329] Alberts and Raff managed to convince Watson that Porter was not a good candidate for authorship of MBC. Among the reasons they gave to him was that Porter was a 'too far advanced, too a senior figure', and fundamentally, that he did not belong to the same 'family' and hence that it was unfair that he was not inhabiting the same roof with them and confronted all the problems that they did. In effect for them Porter did not have at all the same working habits as they had. Rather than being there every day and participating in the networked 'team mechanics' of passing their writings backwards and forwards among themselves for suggestions, Porter only came occasionally to Fort Hill and in addition, he always had a patronising and hierarchical attitude towards the others authors.[330] The solution to this although expected was quite peculiar. To get rid of Porter, Watson had the wonderful idea of placing the blame of the decision on Raff alone. According to Raff, Watson told Porter that: 'Martin Raff thinks you are just not good at this'.[331] Soon after that event Dennis Bray was selected to replace Keith Porter on the grounds of being a cytoskeleton expert.

### 3.2.3. The causes of the 'culture clash': The mechanics of the teamwork writing experience.

It is evident then that Keith Porter was dropped out the team for not having the same working habits and the same entrepreneurial 'team' style, as all the rest had. To put it differently, Porter did not belong to the same 'family', to the same culture that

329 MRI 00.24.15.

330 MRI 00.24.24.

331 MRI 00.24.54.

simultaneously promoted working hard and having fun.[332] Keith Roberts recollection of events confirm this, when he stated that:

> […] Neither Bob nor Keith Porter […] were really working in the way that was going to become the paradigm [?], as collectively as a team passing stuff backwards and forwards, they both have been going off doing their own thing… sort of thing […] their style of working yeah, their style of working, so, they fell by the way side.[333]

The non-experienced cell biologists were fully excited about doing something new for them because by sharing the same practices they became a sort of 'hard-core group'. They also felt unconcerned by the communal lack of expertise on cell biology, none was an exception in this, so none could make each other feel bad about not being experts. Their communal co-produced, co-generated text with each being part of a team and their view of themselves as a 'family' was enough for them to overcome their lack of experience.[334] In fact, from their own recollections of events they remember to have sought more of each other than their partners, families or close friends during the many years they shared together in writing the first edition of MBC. It was therefore unsurprising that they resisted someone like Porter with his sporadic visits and his image as a hierarchical, patronising 'old guard cell biologist'. He never fitted in with their practices as being part of that family and perhaps made them feel uncomfortable about their inexperience as cell biologists. Furthermore, the authors of MBC all shared and subscribed to the innovative vision that Watson had for the book. MBC had to be totally based on concepts and not based on structural cytology or describe countless facts about cells. Porter's style was simply perceived by the authors as incompatible with these objectives.

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332 The terms 'team' and 'family' were constantly used by Raff, Roberts and Lewis during the interviews when referring to themselves in the process of writing MBC.

333 KRI 00.05.20.

334 KRI 00.11.54.

The preservation of the 'team dynamics' had become something of an obsession for the core authors of MBC, Alberts, Raff, Roberts and Lewis (those present from the first 1983 edition to the fifth 2008 edition). The team dynamics was and still is a key factor for the authors to take into account when selecting new authors for the book.[335] Selection of new members has been an ongoing process right from the beginning of MBC and is normally based on very simple criteria. Only those that have written a chapter before, and more importantly 'come to many meetings', as Raff put it, are selected by the core authors to become authors.[336] This was the case for instance with Alexander Johnson and Peter Walter, both from the University of California San Francisco, who became authors from the fourth edition of 2002 and have remained such ever since.

Working as a team also favoured the development of close relationships between some of the authors. Alberts and Raff's consensus to get rid of Porter as an author of MBC was a manifestation of this. In Raff's view, Alberts was indispensable, 'without Bruce no book', he affirmed. Moreover, Alberts was hailed by Raff as 'the smartest', as 'someone special'.[337], and as the 'the more focused intelligent character I know'.[338] Raff knew Alberts in fact long before the production of MBC started. They first met circa 1974 when Alberts tried to recruit Raff to Princeton where Alberts used to work before moving to California and also later from when Alberts spend a sabbatical in London. It was Raff who proposed him to Watson as a potential writer for MBC when Sambrok dropped out of the initial team. He told Watson that Alberts 'will be terrific […] 'he is so bloody smart'.[339] This close relationship between Alberts and Raff had a long-lasting and essential influence for the development of MBC. There was a kind of informal agreement between them that began to grow meeting after meeting.[340] Moreover this special relationship exemplifies what Shapin sees as one of the main important features for the

335 MRI 01.00.20.

336 MRI 00.59.48.

337 MRI 00.51.37.

338 MRI 00.16.55.

339 MRI 00.07.35.

340 MRI 00.12.54.

development of science in late modernity, one that Max Weber anticipated in his famous 'science as a vocation', that of trust; or rather the establishment of relationships based on trust among the members of a working group, on their capacities and moral values as professionals and human beings to advance their objectives and targets collectively (see Chapter 5).[341]

The original plan was to finish MBC in a couple of summers (two years from that original meeting in 1976). It took instead seven years for the first edition of the textbook to be produced. All the authors interviewed agreed that sticking together throughout those years, as a 'family' was key. They formed a solid team, all having a wonderful experience and a gorgeous time writing together (see Roberts' comments above).[342] This 'team' conception of work, with authors learning from each other and posing fundamental questions to each other in a kind of communal life, was in fact one of the novelties of MBC, a completely new way of writing a textbook for biosciences at the time, a strategy that as we saw, was based on Borden's ideas of creating a relaxing working atmosphere conductive to new ideas and creative writing. Writing, as a team was a wonderful experience in Martin Raff's view, he remembered pleasurably the days he sat under a tree and wrote his chapter on immunology.[343]

The team working culture not only had a deep impact on the writers, as a result of passing their writings among themselves for corrections; it was also quite similar to the way networks function. Raff relates that Alberts who knew nothing about immunology 'would, ask fundamental questions' that changed the way 'I would write and think about it'.[344] It was equally very educational for him when he read Albert's chapter on thermodynamics, a chapter that finally never formed part of the textbook.[345] Keith

341 Shapin, 2008, op. cit.

342 MRI 00.41.33.

343 MRI 00.10.08.

344 MRI 00.10.45.

345 MRI 00.11.00.

Roberts also recalls having a great time writing the book especially on where it concernes having the same objectives of 'being part of a team' or even 'a family'.[346]

### 3.2.4. How to write MBC: The novelty of 'concept headings'.

In expanding the style Watson already had developed in MBG the idea was that MBC had to be written 'conceptually', using straightforward 'concept headings'. Raff explained: concept headings were about saying very simple things like: 'the nucleus is round and is in the middle of the cell and then you write a little bit on it'; a way which doesn't look that different to the way books for young children are written.[347] In Watson's own words concept headings were about the use of 'boldface sentences to summarize the main ideas covering paragraphs below'.[348] Similarly, Roberts' views concept headings as short, didactic type of statements that organise the text into 'bite-sized and digestible sections', which are normally associated to images, so clarifying, extending or illuminating the text. [349] In concept headings the title became an affirmation that then gets explained (and even repeated sometimes in the main text and in the legends of figures). Julian Lewis thinks that it was Bruce Alberts 'who very strongly set the tone that the book should be conceptually interesting and that it should try to explain mechanisms and should not burden people with unnecessary facts', He even thinks that they 'went quite rather far in that direction, so avoiding naming names sometimes …..[?] and Bruce's boundless energy […]'.[350]

Concept headings were in Raff's view a real revolution in writing at the time. He even considers that its use in MBC has been so innovative and important that ever since most books on cells as well as scientific papers have adopted that style of writing.[351] The

346 KRI 00.11.54.

347 MRI 00.13.09.

348 Watson, 2007, op. cit., pp. 218.

349 Roberts, 2003, op. cit., pp. 437.

350 JLI 00.07.40.

351 MRI 00.13.00.

team thus quickly made theirs Watson's original vision on how to write the textbook 'conceptually' by using concept headings as opposed to a dry factual description. Of course this writing posture was not as straightforward as it looks and was not taken on board at the same level for everyone. Watson for instance despite his insistence on concept headings thought that, 'the more facts the better', 'because you want to give the student a feeling of how much they know, right, that this is not just you making them up'. Raff himself has been in the opposite side 'the fewer facts the better'.[352] Raff further clarified how the whole process worked: 'everything we'd write should have a story, it should be interesting, it should have a reason, don't learn a fact unless there is something about the fact that helps advance the story, so a lot of it was speculation'.[353] Raff's comments unveil a couple of important differences between MBC and former textbooks in the discipline such as CB. The first one, is that, whereas there was a significant amount of speculation about cellular processes in MBC, that was far less the case for former textbooks as CB, a textbook that was far more cautious about claims on cell functioning that were not fully proved experimentally. The second important difference highlights a key difference between the practice of cytology in the 1950s and the practice of molecular cell biology in the 2000s. Whereas the writing in CB was by and large 'fact driven', in the case of MBC it seems that the story is equally or even more important than the facts. Roberts currently thinks that the real risk with MBC was about being 'totally conceptual' and not laden down with history or names, 'it was where the science was as far as we could tell at any point in time…you know, definitely'.[354] The significant stress by the authors on crafting an appealing story with as few facts as possible, with no history or names, is in my view, a wider phenomenon that exist beyond the production of MBC. It is indeed a trend that also began to characterise society from the 1970s onwards, one where the image began to displace the object (see Chapter 6).

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352 MRI 01.22.06.

353 MRI 00.35.42.

354 KRI 00.12.25.

Sharing the same writing objectives and having developed the same writing practices and styles as a result of being together during the six weeks summer retirements periods each year, allowed the authors to acquire another feature that in their view is unique to MBC: the writing 'with one kind of voice'.[355] In effect, despite being a multi-authored textbook, and treating subjects as diverse as DNA replication, the cytoskeleton and the immune system it is quite easy to sense when reading it a kind of homogeneous and unique voice running throughout the chapters of any of the editions.[356]

Another important issue at stake when MBC was planned was to delineate what would be its epistemological content, an issue for which Watson again had an answer. In his view this was simple: the textbook would integrate 'microscopy' with the new molecular biology and biochemistry and thus correct for all the wrong paths textbooks were taking at the time, that of teaching a science that was no longer being practiced (see Chapter 5). Most importantly, the spotlight had to be placed on themes that were close to the experiments that were going on in the labs, those that belonged to the growing process of molecularisation.[357] Above and beyond the agreement the participants in the second London meeting reached, and that was confirmed at further occasions, was that the textbook should play a key role in speeding up the process of molecularisation of cell biology by bringing closer together its teaching and its laboratory practices.[358] Succinctly put, in the authors' opinion, MBC had a corrective role to play, one that would modify what has been done so far in the labs by imposing a new way of doing and a new way of viewing how cells work. The achievement of the epistemological goals of MBC was reassured by the networking functioning established among the authors and other groups such as teachers and students. This fluid networking practice was based on a constant feed-back process at play at different levels; among themselves and among students,

355 MRI 00.35.13.

356 Different to CB when from the 1975 edition onwards the cytological chapters were written by a microscopist and the molecular ones by a molecular biologist.

357 MRI 00.02.45.

358 MRI 00.05.45.

teachers and scientists from other labs (warranted as we saw above by the work of Borden and Robertson).

The team's based networking writing experience was initially based on a literal division of labour. The general initial consensus on who was doing what was achieved by each author writing a chapter or two on the areas of their speciality.[359] Thus Raff was going to write a chapter on immunology and another on cell membranes, Alberts on molecular genetics and Roberts on plants. The agreement was that everything else, what the authors did not dare or did not want to write about 'would be bought in from experts' who would write the chapters for them.[360] Outside the team, experts received around 10.000 US dollars to write a draft of a chapter. Those who just read and commented on a chapter got 200 US dollars plus a copy of the book when published.[361] In more detail, the chapter writing process worked as follows. The articles written by the authors once finished circulated back and forth among them for suggestions and corrections. Those articles written by outsiders were re-written by any of the official authors, usually Alberts and Raff, then went back to the original author and finally went to Miranda Robertson who after adding her own corrections would present them to students and teachers.[362] The whole feedback process, depending more or less on the particular chapters, went through several cycles. The process of gathering outside opinion on how to improve the textbook is one, which has never stopped and on the contrary it has since expanded. Roberts commented to the author that they organised (supposedly in 2005) in San Francisco a meeting that gathered 'twenty top cell biologists from around the world, all met there for a whole day session going through what people thought the book should look like in the next six years time'.[363] This constant interaction with specialists also allowed the 'team' to avoid controversies over, for instance, which model, if there was a choice to make between two or more competing ones, to put in the book for explaining a given

359 MRI 00.02.59.

360 MRI 00.03.05.

361 MRI 00.40.10.

362 MRI 00.33.34.

363 KRI 01.11.42.

phenomenon. With this mechanism of a 'pre-formative consensus' in place, the authors warranted that the book's imagery resulted in being approved by the largest possible number of specialists on the field. To put it simply, by creating consensus before publishing they were standardising the latest form of molecular imagery in cell biology.

### 3.2.5. On hidden networking and its consequences and the importance of telling 'sound' stories about the unit of life at the textual and the visual level.

Scientific networking refers to the written and personal interaction among a group of scientists concerning their research problems working in a similar field of research. Although not new, the practices displayed to produce MBC took scientific networking into another dimension. Essential as we saw, was the enormous number of scientists that in one way or another got involved in its production.[364] One emerging feature is that the number of 'collaborators' is massive when compared with those in De Robertis et al of 1980 and 1987). By looking at the quality of the interaction among the authors of MBC and their collaborators it is possible to find some clues about this difference between both textbooks on this matter. Several subject specialists got into frequent contact with the authors in various ways and throughout the successive editions. They sent pictures and/or pieces of writing almost as big as full chapters together with accounts of what the main research lines in their labs were, including the results of their latest experiments.

One of the most peculiar results of this network of collaborators, that I dub as the 'hidden collaborators', was the fact that they received in exchange from the authors of MBC not only feedback on their written work (normally papers in the process of being sent for publication), but suggestions about untested experiments they had not thought about. As Raff recalls 'we were well connected between us to most of the scientific community'.[365] To which he added.

> We were shocked at how little was known. I mean fundamental things that would be easy to find out have never been asked, never been done, so we would

364 The number of scientists that the authors acknowledged in the different editions only kept increasing throughout the successive editions.

365 MRI 00.36.50.

> call up at the experts and say: Do you know what is the half life of this protein?… [the reply ] (I don't know). Don't know? Why is it that you don't know, could you do it, could you find out? It would be very useful to know when we are telling the story.[366]

Raff thinks that this process had even deeply influenced his thinking in science.[367] In view of the mechanics of this 'hidden networking', it is not an exaggeration to affirm that in many areas the making of MBC acted as a catalyst of research with a key and decisive role on its direction played by its authors.

Roberts also remembers that during the process of writing the different editions of MBC, Alberts and Raff suggested key experiments to do for their colleagues.[368] Both were well and widely connected with scientists working in related fields because they passed a lot of their time reviewing other colleagues' works. Moreover, when Alberts and Raff revised manuscripts as part of the peer review process or informally outside the journals involvement, apart from the suggestions of ideas and experiments, some of the data from those papers were presented 'as gospel in the book before they became even published (in scientific papers)'.[369] Curiously enough an issue that at the time never presented problems of plagiarism. Of course this practice of using data that was sometimes even sometimes transformed in imagery has diminished considerably because of the shortening time between the time of submission of a manuscript and its publication. Although eventually used less frequently this has always been a feature of the book. As we will see below when discussing how MBC was reviewed, this was noted by many in the field and even labelled as 'speculative thinking'. Roberts went further on this and admitted that you have to be very careful with this way of doing things because in his view: '90% of the literature that comes out is likely to be wrong or unrepeatable or wherever'.[370] Roberts admits that: 'Yes, there have been several things where things have

366 MRI 00.35.56.

367 MRI 00.36.33.

368 KRI 01.08.15.

369 KRI 01.08.15. My remark in brackets.

370 KRI 01.09.20.

been put in where… perhaps it wasn't a huge amount of data at the time , yeah…I don't think many of them turned out to be wrong'.[371] Although there is not a precise sense of proportion of the extent of this 'speculative thinking' Roberts recognised that there was a few that they got completely wrong, such as the visual and epistemological conceptualisation of the Golgi maturation processes. They conceptualised it as a vesicular transport instead of a process of cisternal maturation, which is currently accepted as the proper model. The existence of this vast network of hidden collaborators and its resultant mechanism of research promotion is related to a further emergent aspect that characterised MBC, that of the importance given to the presentation of well-nuanced stories about the unit of life; an aspect that as I remarked earlier went to characterise the discipline of cell biology from the 1980s to the present time.

When the first feedback from teachers who had read the first of a series of chapters of the textbook began to be available to the 'team', two main comments featured that the 'level was too high' and that the book was 'too conceptual' with 'not enough facts'.[372] In Raff's view this last comment meant that the authors' way of 'contextualising facts' was not very well received by the readers and hence was not working well. In his own words:

> We agreed that we wouldn't give a fact without putting the fact into some context to tell us….what could a fact mean. If we didn't understand what a fact meant you would tell a little story what it might mean, why is it good for the cell to do it this way, why you would do it this way when you could do it six other ways that seem simpler or more elegant or something.[373]

Raff links the telling of stories to the process of speculation and gives a justification for it when he states:

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371 KRI 01.09.50.

372 MRI 00.17.30.

373 MRI 00.17.33.

> So, there was a lot speculation in the book, there still is quite a lot of speculation in the book and at that time there was no story, I mean there was hardly anything where you really understood, how something worked, and so you were making up these stories in an alarming rate but still seems sensible to do it that way because it will be interesting, so everybody agreed that was interesting. [374]

As the two former passages reveal, for Martin Raff speculation was one of the main and exclusive attributes of MBC and hence something to praise. Speculative thinking and making a 'gospel in the book' of an experimental output 'before it became published', as Roberts put it,[375] did not bother Lewis at all either, who while conceding that sometimes they had gone 'quite rather far in that direction', felt that 'they should not at all apologise for that'.[376] For it does nothing that they were particularly guilty of 'saying things were fact when they were not'.[377]

The importance given to the telling of a well-nuanced story in MBC applied also to its imagery. Former textbooks like CB imported images from other authors without changing them.[378] Although other author's images were valuable because 'they were original data', to have put them in a 'unmodified' way, would have been catastrophic for the case of MBC, Roberts commented.[379] One novelty used in the making of MBC was that the phrases that described the image on the figure was almost the same as that used on the text as a way of reinforcing the message. The most important novelty brought on by MBC is that its imagery was able to tell a complementary story to that on the text, one

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374 MRI 00.18.05.

375 KRI 01.08.15.

376 JLI 00.08.15.

377 JLI 00.08.54.

378 Recall the sliding model for muscle contraction and lipid bi-layer model for the cell membrane originally proposed by Davson and Danielli in 1935 and further expanded by Singer and Nicholson in 1972. See Chapter 2, subsection 2.2.1.*'The development of molecular imagery inside CB: Some relevant aspects of its visual and epistemic content before the third wave of molecularisation of cell biology (1940s to the 1970s)'.*

379 KRI 00.18.36.

that could run almost independently. Keith Roberts is of the view that 'you are in trouble if you cannot move backwards and forwards between figure and text'. In his view, 'figures have to tell one story and you need to be able to get at a figure or to understand a figure within a few seconds' so in a way they carry a parallel text.[380] In Roberts' view Bruce Alberts is a perfect example of this since, he was able to understand what is going on by looking at the figures without looking at the text. For him (an attitude that was expected for all readers) there are two versions of the text, the textual and the one constructed with images. What is more, by looking at the imagery in display, in Roberts's view 'you should get a good feel for what the things are about'.[381] Roberts thinks that 'the written text and the illustrative text should both carry not only the same message but the same message in different ways', so that 'you can understand it's coming up… the concept from two different ways, and so, it should be as simple as to tell the story and nothing more'.[382] Lewis, the less image oriented author, also recognises not only the importance of images for the production of knowledge but their independence from the text to tell a story. He is aware of people that have read the book by looking only at the pictures.[383] Lewis remarked: 'Pictures are very memorable […] to the same extent it is easier to remember a picture than a piece of text' […] pictures are a huge aid to memory'.[384]

### 3.2.6. The role of Keith Roberts in creating the images of the third-order visuality: 'or the handiness of having an artist in the family'.

The person who created the images for MBC is Keith Roberts, former Professor at the John Innes Centre (an independent research centre) at Norwich, UK, currently retired, but, still active as a curator of several exhibitions on the interface between art and

380 KRI 00.18.35.

381 KRI 00.19 52.

382 KRI 00.20.08.

383 JLI 00.35.48.

384 JLI 00.36.00.

science.[385] Roberts completed a PhD in biochemistry at the University of Cambridge and had even from his previous years as a secondary schoolboy an active interest in art. Despite further schooling in sciences he always managed to keep that interest alive by following many arts-related courses while doing his university degree. As a teenager he was also very keen on architecture and microscopy. He got very exited while telling me the story of the time when he could afford to buy his first optical microscope at the age of fourteen and set up a young microscope club in Ipswich, where he used to live.[386] Concerning his pictorial work, before creating the imagery for MBC, he created the images not only for Watson's MBG but for many other textbooks over the years. Among the books he illustrated are: John Kendrew's *The thread of life* in 1966, the renowned, Albert Lehninger's *A short course in biochemistry* in 1973, as well as many cartoons presenting molecular interactions for the scientific journal *Trends in Biochemistry (TIBS)*.[387]

Roberts' talent at drawing and his aesthetic sense of things are recognised by Raff, who remarked that:

> Keith, is an artist as well as a cell biologist and that of course has been a huge component to the success of MBC […], so Keith is really a genius at taking complex concepts and putting them into an aesthetic and simple diagramatic form.[388]

Concerning Roberts' qualities as manifesting during the writing process Raff said:

> We would write rough diagrams and Keith would then turn them into these really lovely things, it was very inspiring for us, you know you take your scratching little diagram that was incomprehensible even to yourself and he would turn them into something really quite lovely and you can see the potential

385 He recently contributed as part of his membership of the identity project on the exhibition 'Identity: Eight rooms, nine lives' (26th November 2009 to 6th of April 2010 at the Wellcome collection in London.

386 KRI 00.50.55.

387 KRI 00.50.10.

388 MRI 00.03.53.

that this could be terrific to work with somebody who was a cell biologist as well as an artist, it would be just terrific.[389]

Roberts' qualities were also recognised by Lewis. During the interview, after flicking throughout the pages of the fourth edition (2002) and finding one of the images produced by Roberts, an image that 'presents' how detergents solubilise membrane proteins, Lewis commented that, this is one of the images where Keith is 'very nicely telling a story about how a mechanism works'.[390]

### 3.2.7. Working with Keith Roberts: Some more insights on the team-network dynamics.

So, it is clear that having Keith Roberts as a co-author, an artist as well a scientist would play a key role for the success of MBC, but there was something else about him too. Roberts was a charismatic and trustworthy character, one that had as a plus a very good sense of humour. Julian Lewis remembers that at many instances during the writing of MBC, especially when the team morale was low, Roberts 'was very good at injecting humour in a subtle way'.[391] Looking in more depth at the working relationship between Roberts and the other authors some relevant issues emerge on the production of MBC. The first one is that every author of the textbook had his own arrangement for working with Roberts.[392] At the beginning and almost in every situation they would bring him a section of a chapter as they wrote it.[393] Roberts would go through those pages and said 'I think we can make a figure here' and suggested to the authors where it would be convenient to have that figure in relation to the text, with this process moving backwards and forwards several times.[394] This original arrangement of interaction changed slightly

389 MRI 00.11.15.

390 JLI 00.23.28. He refers to Fig 10-26 in Alberts, et al. 2002, op. cit., pp. 600.

391 JLI 00.18.53.

392 MRI 00.52.31.

393 MRI 00.52. 45.

394 MRI 00.52.57.

however as he began to get busier with 'more and more chapters rolling off' and with an increasing numbers of images to put in.[395] Raff found it sometimes strenuous and frustrating working with Roberts under these conditions. In his view:

> Keith, is… he… he's 'got 'an attention… problem, you know, he can stick with something for 5 or 10 minuntes but if something….a bird flies, you know, across his vision he is out there with his binoculars looking at… you know, and if you are waiting for a figure to move on, it… that drove me nuts absolutely nuts, I couldn't do it, it was just too frustrating so I found a way of working with Keith where I would draw the figures in a very rough form with some colours […] I'll give him the end of a chapter I'd give him a chapter, text and I'd give him give the drafts and where the figures were and then he will go away with that and he would work out his way of doing the figures.[396]

The overall impression when discussing Roberts' pictorial abilities with Raff is that Roberts had a magic touch on things. Commenting on his drawing style Raff stated that: 'He just transforms a piece of 'shit' into something that looks nice and it is much easier to read, it's just simpler'.[397] To which he added:

> When he does the figures he would never agree to do the figures until you give him something that you have written, so, he wants to know, you know, what has been written, where the figure fits what is actually trying to say, before he'll be willing to start to draw, so, he is a fundamental part of this […] Most people when they do books they harvest the figures from other books from the literature they don't do the original drawings, […] so it is very unusual to have one of the authors to do the art.[398]

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395 MRI 00.53.10.

396 MRI 00.53.28.

397 MRI 00.55.10.

398 MRI 00.57.18.

This last was in fact an essential feature for the success of MBC. Whereas the 'team work' during the writing guaranteed a sole and common voice running through the text, a single 'authorial voice', the work of Roberts warranted that the same was true for the visual, a single authorial imaging.

Not all the other authors because of their different working style had the same kind of relationship Raff had with Roberts during the writing of MBC. Alberts for instance would give to Roberts text with more elaborated images. He did the figures as he wrote the text.[399] In other words, Alberts wrote the text around the figures, either his or those from Roberts. Most of the other authors Bray and Lewis did it the other way round, that is, they wrote the text (sections) first and then went to Roberts with that text sometimes including a little sketchy drawing of their own. In every case however, Roberts then did the final design of the figures.[400] Julian Lewis had also a completely different style of working. Basically 'he doesn't like figures, figures are for him just an afterthought', opines Raff.[401] Lewis' cultural–scientific background was different from all the others. In Raff's own words, 'he brought a style that

> Is entirely different from the rest of us as, he begins from first principles, he is a physicist and a mathematician, so that before he start to write he goes back to the atoms, he needs… to understand… you know from [?], is just a different style'.[402]

From Julian Lewis's own recollection of events concerning his working relationship with Roberts, he agrees with Raff that at the beginning the interaction with Keith was less close over the figures for his chapter. It seemed to him that Roberts was normally overburdened, because he had all the illustrations to make for the book.[403] In

399 MRI 00.55.35.

400 MRI 00.55.42.

401 MRI 00.55.50.

402 MRI 00.58.05.

403 JLI 00.09.45.

addition the kind of images Lewis worked with (images of developmental processes) were somehow of a different nature than those from the others. This placed him in a

different relationship with Roberts since Lewis tended to do more detailed drafts for him than the others authors. Lewis recognises that as time passed by, he learned to interact and work better with Roberts. In this regard Lewis commented that:

> If you give him something that is too finished then he just takes the finished version and touched it a little bit, if you give him nothing at all to work on to start with, then he cannot get started, so the idea to work with him is to give him the right amount that he knows what to do that brings his creative skills to there […] he has this special [?] he can make the message much more strikingly than otherwise…[404]

It was only after many rounds of interaction with the other authors and by carefully examining their sketches that Roberts would come up with suggestions about the images.[405]

Overall, both Raff and Lewis highlighted and praised the open and relaxed predisposition Roberts adopted to the different working styles of the other authors during the writing process, a predisposition they both appreciated and that was key for the smooth working relations of the team. The working relationships between Roberts and each of the other authors seems to have been so smooth and pleasantly convivial that neither Raff nor Lewis could remember any significant disagreement over the creation of any particular image with any of them. There was never something like a complete refusal of any image he or any of the members of the team created or any situation that might have created tension among them.[406] That said, Roberts recognises that the image on homologous recombination is probably the one that triggered quite contrasting positions among the authors and hence one that took more time to reach an agreement upon.[407] This image presented a problem for the 'team', in particular in the latest edition

404 JLI 00.10.55.

405 JLI 00.12.04.

406 JLI 00.39.28.

407 KRI 00.39.36.

of 2008, for each author felt that none of the images produced fully captured the phenomenon. Even though this represented a real struggle it never reached the level of a heated discussion.

A related aspect that Roberts remembers well is having some demanding and challenging moments as an illustrator due to the different manners of viewing things. Working with Alberts for instance, the more demanding of the authors due to the nature of his ideas for images, was the one with whom most intense engagement was required.[408] Roberts remembers a particular instance from his interaction with him. Alberts wanted to show in his chapter on bioenergetics how proteins, ('protein machines') can do work in a coordinated and mechanical manner; how they get assembled sequentially from preformed units after detecting an energetic change on the substrate molecule to do a bio-energetic job and as a consequence change their conformation. Alberts wanted a particular way of visualising these 'protein-working machines', one that would show his conceptual opposition to a casual molecular colliding process. It took some time but finally 'the 'safe cracker', (how they called the image for themselves to highlight its coordinated way of opening safety boxes with the key) was born **(Figure 27, A)**.[409] For the creation of these kinds of 'totally conceptual images', as is also the case with the 'walking tooth' **(Figure 27, B)**.[410] Roberts comments that: 'we sort of invented that one again chatting with Bruce you know, it came through chat… was… exactly what do you want to say and then try to draw it'.[411] But again, despite the different working styles and approaches to images, working with Bruce, was quite a rewarding and pleasant experience in the end for Roberts.

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408 KRI 00.41.15.

409 Alberts, et al. 1989. op. cit., pp. 132, Fig 3-64. 'A protein machine', also in Alberts, et al. 1994, op. cit., pp. 212, Fig 5-26 'A protein machine'.

410 Alberts, et al. 2002. op. cit., pp. 184, Fig 3-75 and 3-76.

411 KRI 00.41.15.

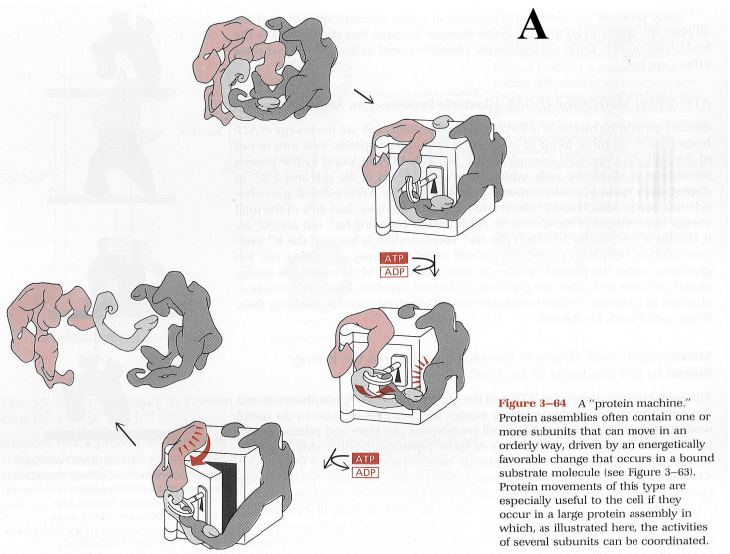


**Figure 3–64** A "protein machine." Protein assemblies often contain one or more subunits that can move in an orderly way, driven by an energetically favorable change that occurs in a bound substrate molecule (see Figure 3–63). Protein movements of this type are especially useful to the cell if they occur in a large protein assembly in which, as illustrated here, the activities of several subunits can be coordinated.

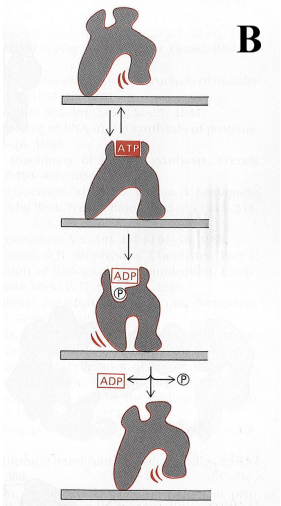


**Figure 3–63** An allosteric "walking" protein in which an orderly transition among three conformations is driven by the hydrolysis of a bound ATP molecule. Because one of these transitions is coupled to the hydrolysis of ATP, the cycle is essentially irreversible. By repeated cycles, the protein moves consistently to the right along the filament.

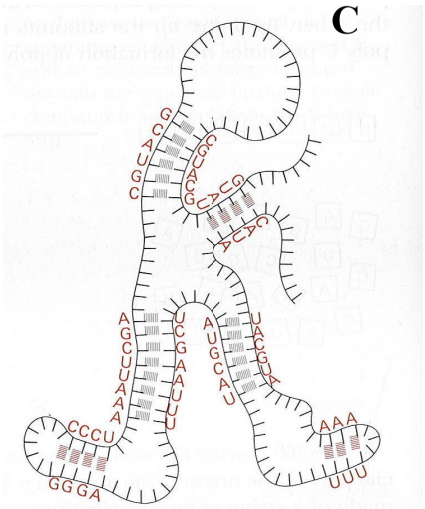


**Figure 1–6** Nucleotide pairing between different regions of the same polynucleotide (RNA) chain causes the molecule to adopt a distinctive shape.

**Figure 27: Anthropomorphic molecules. A) The 'safe cracker'. B) the 'walking tooth'. C) the 'human RNA'.**

**Alberts et al 1986**

### 3.2.8. Roberts' positive and negative influences for the making of MBC.

Keith Roberts recognised that the development of his image creation style had many influences both positive and negative. The most obvious positive influence from the scientific side is to be found in his previous participation as an illustrator in MBG. He sees the transition from MBG to MBC as a process of professional maturation, one that by moving from prokaryotes to eukaryotes allowed him to increase his visual qualitative repertoire. Moreover, without any doubts the 'double helix', especially the two ribbons depiction made by Odile Crick (Francis Crick's wife) for the original 1953 paper, caught Roberts attention and began to act as a model for his style in the creation of images for the molecular culture.[412] He was amazed about the capacity of that model, 'with the absence of enough robust data to pin it all down' to capture 'all the conceptual points of the proposed structure in its simplicity'.[413]

The other positive influence related to science came from other textbooks, especially from the imagery displayed (mainly 3D models of molecules) in two biochemistry books that were very popular among students at the time (1960s and 1970s) that of Lehiningher and that of Stryer.[414] As he put it: 'Stryer particularly in the sense of the illustration programme, clear, crystal clear, came about 1975, it was exactly at that point where something captured the imagination… full of colour and beautifully done at that time'.[415] Roberts also remembers his excitement about the experience of drawing ribosomes for the production of the second edition of MBG. Watson got sent electron microscope images from Aleksander Spirin, a Russian structural biologist and passed them to Roberts to do the first drawings of these sub-cellular particles involved in protein synthesis.[416] Roberts committed himself to work hard with them, he saw a lot of these

412 Roberts, op. cit., pp. 440.

413 Roberts, op. cit., pp. 442.

414 Lehninger, 1982, op. cit.

415 KRI 00.14.15.

416 KRI 00.26.00.

little particles and as he put it 'I 'eyeball averaged them'.[417] He further commented that at the time:

> Nobody knew how a ribosome looked like […] If you are going make a little icon for something you may as well make it the right shape, it seemed, I don't know it just seemed a sort of… common sense really it just seemed common sense and the more I thought, I think about it, I don't know you just drew what you have to draw that is the way it came out.[418]

From that experience with ribosomes onwards many of his drawings would become dependent on electron microscopic images. This dependency was so intense that he admits that as time passed he felt he 'became an electron microscopist' himself.[419]

A very important positive influence for Roberts' style came not from science but from the arts, or more precisely from a book on the relationship between science and art, *A new landscape in art and science* by Gyorgy Kepes a Hungarian born painter, art theorist and Professor at the College of Visual Arts at Harvard (1963). Roberts remembers that just before going to work with Watson he was on holiday in France with his parents and felt captivated by a book he saw sitting on top of the towels of an artist friend of his parents on the beach. When the artist came aware of Roberts' interest on Kepes's book, he lent it to him. Roberts swam not only in the sea with delight that summer but also in Kepes's book. Roberts recognises that *A new landscape* was a 'very, very influencial' book for him.[420] Kepes's textbook had 'lots and lots of illustrations of scientific things that have artistic interests' and was written by authors from different backgrounds.[421]

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417 KRI 00.26.39.

418 KRI 00.34.09.

419 KRI 00.34.20.

420 KRI 00.24.15.

421 KRI 00.24.50. He still has Kepes book in his current studio in Norwich and gets a glance at it every so often.

He relates the importance of Kepes' work and the influence it had on his own pictorial style to a particular historical moment (during the 1940s-1960s) when due to the emergence of a panoply of new photograpic techniques suddenly people became able to see what could not be seen before. When asked about this he answered:

> That in a way to me is the most fascinating part of the whole process in a way its making concrete that which is, but is too small… it is why that book by Kepes […] the point of that book […], the new landscape, […], it made me realise […] what he meant by the new landscape was that both artists and scientists alike and the general public suddenly had access in the sort of middle part of the last century to a whole set of images of things which they could have never seen before. So there were x-rays photographs of flowers and people you know, there were time lapse pictures, you know, of very fast object you know, like the famous bullet going through a light bulb and that or through a playing card, you know, quite famous, or the milk drop, you know. All these things, very fast photography, time-lapse things, change movement, and there was astronomy you know you are suddenly seeing things that could never have been seen by any other generation of human beings […]. And Kepes I think, was one of the first peoples to appreciate that was an unbelievable rich vein of visual imagery that has been bought into by artists, and , and…and…that is the theme that has been taken up by Waddington in his great book on art and science […] , you know its…so, I think that was a really important book and I think that the whole idea of being able of seeing the unseen is certainly what made me and my science […] trying to visualise and uncover the structures of … structure was important.'[422]

Although referring to phenomena that were concealed from view rather than invisible, such as the milk drop (invisible because they happen too fast to be detected by our senses), or the images of bones with x-rays, which again are not invisible *per-se*, but because are just hidden from view, it is undeniable the influence that this idea of

422 KRI 00.24.20.

unveiling something which is out of view, would have on Roberts for the depiction of things that are invisible.

As in any creative enterprise the imagery created by Keith Roberts in MBC also derives from some negative influences. CB, the textbook by De Robertis et al (the 1980 edition) was not at all the sort of book the authors of MBC wanted to do at all, so it did not influence them in any way except in setting their own standards on how not to make their own one.[423] They identified two problems with textbooks like CB. Firstly, it was too cytological, too based on electron microscopy and secondly, it lacked that common voice running behind both the textual and the visual story. Another 'negative model' was the textbook, from Mahler and Corder *Biological chemistry*[424], a standard book in the UK at the time. According to Roberts, 'anything we did not want to be is that turgid catalogue of facts with no conceptual underpinning, no liveliness, no engaging at all…' He recognises that although quite a popular book Mahler and Cordes was 'as bad and as awful as you could get'.

### 3.2.9. The importance of having a coherent illustration program to back up the epistemic claims: Roberts's five rules of depiction.

It was clear that for MBC to be successful Roberts had to organise and put in motion a solid and coherent illustration programme to back up its epistemological claims. The main idea of having a coherent illustration programme is expressed succinctly by Roberts:

> When you open a book and flick through it you wanted it to look the same, you wanted it to look […], so that the illustrations look as if they have one authorial voice just as you would the text, so, […] you can really be honest to know who is writing which bit of text, because it is supposed to speak with one authorial voice and likewise the drawings, you want them written with an authorial voice

423 KRI 00.14. 49.

424 Henry R Mahler, Eugene H Cordes, *Biological chemistry*, New York Harper and Row, 1971.

> […] You don't want lots of illustrations from different people crowding the message because you are getting different voices and therefore conflicting.[425]

In a similar vein, Lewis acknowledges the special awareness and the efforts 'the team' put into either not making the images too complicated or having too long sentences in their legends. [426]

A coherent illustration programme is also what separates in Roberts's view a properly authored textbook from one that just jots images from other people in their chapters, arguably such as CB. Roberts does not remember from where they got the idea, but what he is certain about is that no book at the time had that style of a combined unique voice and unique imagery throughout it.

The illustration program that Roberts created when doing the images for MBC was based on five 'pragmatic' rules of depiction.[427] The programme looks in a reduced form as follows:

I) Illustration programs need to be unified or consistent throughout the book.

II) A figure should tell only one story, as economically as possible.

III) Pay attention to scale, it has to have consistency throughout all the illustrations.

IV) Use color only to contribute to the overall feel and coherence of a text. Don't use when not needed.

V) Think carefully about ways of in which figures can tell more than one story (link, reinforce, remind, revise, summarise, or just simply add a welcome touch of light relief).[428]

The rules were originally developed for Roberts's personal guidance. Because of their success they later became incorporated in the Garland publisher editorial depiction

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425 KRI 00.21.04.

426 JLI 00.20.45.

427 Roberts, 2003, op. cit., pp. 439-40.

428 Extracted from a document that Roberts provided to the author during the interview.

rules to follow for the creation of images for other textbooks in biology.[429] Furthermore, they also became the subject of talks at meetings given by Roberts on many occasions and throughout the years on how to create successful scientific illustrations. Roberts's imagery and his illustration rules were pivotal for MBC, so pivotal that as Lewis remarked:

> There are quite a few people who read the book basically by looking at the pictures and not struggling too much with the text, and …yes, certainly […] a picture is very memorable is quite easy in a sense it is easier to remember a picture than it is to remember a bit of text […] so, pictures are a big aid to memory […] a vivid way of conveying ideas.[430]

No doubt then how important the consistency of the illustration program and its five rules of depiction were for making MBC an easy and compelling reading for students.

### 3.2.10. Challenges to the illustration program: Computers, Color and GFP based confocal microscopy.

Between the first edition of MBC in 1983 and the third one of 1994, many changes occurred at different levels, the most important one being the extensive use of computers for graphics and molecular modelling, the use of colour in printing and new visualisation techniques such as the combined use of green fluorescent protein (GFP) and confocal microscopy. Although normally technological innovation is supposed to have a positive impact on the field in which it is applied, it is worth pondering if computer use and the resurgence of microscopical culture in cell biology, through the use of GFP and confocal microscopy, entailed a negative impact on the molecular imagery created by Roberts.

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429 Material offered by Professor Roberts to the author during interview.

430 JLI 00.35.49.

Beginning with computers, Roberts has never used them for the creation of images. All of his drawings were and still are made in fact by hand.[431] What they did though in the context of MBC production was to speed it up the whole process of creation of images. It was during the hayday of computer use in the early 1990s that Nigel Orme started as a new member of the illustration team of MBC, the time when the team as they put it in the preface of the third edition (1994) 'ventured into full color'. Orme joined 'the MBC team' at a time of significant turmoil in printing set-ups practices at editorials. The preference of these new printing strategies was a situation that could have threatened Roberts's drawings and imagery programme. In the end however computers and the concomitant use of color finally converted Roberts' drawings 'into more easily 'printable colour art work', but nothing else.[432] By looking a bit more in depth though it seems that both computers and color had a different impact on the way the images for MBC were produced. Whilst computer use facilitated the process of image production, colour introduced some significant difficulties for this process. The use of computers or 'the electronic way' of doing images, as the authors described it, entailed Roberts making the drawings and Orme transforming them into images for the computer by using the programs 'Illustrator', 'Page Maker' and to a lesser extent 'Photoshop', for the page layout. As anticipated, the main effect was to speed things up, because of the facility to change things when they were wrong. Concerning the speeding up process, Raff recalls having, during the writing of the first edition, 'runners', that is undergraduate students who volunteered to go to libraries with a list of references suggested by the authors and photocopy images from papers. Even if handy at the time this became an unimaginable process to use these days when with a computer at just the click of a button you can have it instantly in your screen.[433] Moreover, before the use of computers, and the 'internet' every figure went directly to a drawing studio in New York by post. Figures were overlayed, with every colour, including the text having a layer, and that was redrawn in a larger form on black Indian ink on separate transparent sheets. So that every time that a correction was needed, it had to go backwards and forwards and that took a long, long

431 KRI 00.31.10.

432 Alberts, et al. 1994, op. cit. Preface.

433 MRI 01.12.37.

time. By the late 1980s as the pace of publication kept increasing this way of working became unsustainable. In order to keep a nice and productive atmosphere despite the changes it was very important that Roberts and Orme knew each other from before. Not only that they were almost neighbours in Norwich, where they used to live, but that Orme also had an artistic background like him, so that there were plenty of ideas to share between the two.[434] Fundamental for the avoidance of computer use having a negative impact on the production of images was the fact that Nigel Orme stuck to the tradition of hand-drawing initiated by Roberts (who, as we saw continued to work that way) and kept going with his ideas of 'conceptual drawings'. Raff's memories on the issue, confirm that Orme made his drawings, even those of molecules, ribbons style, which were normally done with the help of computers in those days, by hand, following Roberts method.[435] So, the novelty, and changes brought about by the emergent computer technology, the speed and the colour, never really put under threat the conceptual way of imaging and the coherent program that was behind it and that Roberts cultivated with so much fondness. Despite the ample possibilities of using computers to produce molecular imagery as the years passed by, Roberts preferred using his hands. He thinks that working by hand:

> Is freer, is easier to think of what you want by sketching, is easier… and then what he does [Nigel] is, he scans it, he scans the drawings and then I do import it into Illustrator as a template and then he does the accurate things over the top of the template […] I would do a drawing reduce photocopying, color it and then give it to Nigel, who continued with it until the final version, the one that would go into print.[436]

As remarked earlier, when the authors wrote the preface of the third edition (1994) they stated that they 'have ventured in full color'.[437] Venture is perhaps quite a optimistic word to convey what was in reality a cumbersome task. In effect, the colour

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434 MRI 01.08.34.

435 Example Alberts, et al. 2002, op. cit., pp. 142. Fig 3-13. (MRI 01.08.59).

436 KRI 00.33.08.

437 Alberts, et al. 1994, op. cit. (Color in American English).

adventure entailed that every figure had to be rethought and remade.[438] It is not that difficult to envisage how burdensome this could be for a book that in average had more than one image per page (1.12 images per page), and 1142 pages in total; no doubt that this signified a huge job to do. In fact they could have used colour well before with the second edition (1989), as Raff recalls, financially this was not a problem. Borden, as expected by 'the team', was there for any cash injection the team might need and the technology already existed. But, because of the labour involved in redoing every figure, all the authors and in particular Roberts resisted it.[439] For the third edition things changed, the production of the book in colour became imperative, as MBC would have looked an outdated book otherwise, as Raff recalls. 'colour gives you so much leeway and of course it looks so much better […] colour was a big advance for us'.[440] Essential to the use of colour was its consistent use, as Roberts himself proposed. He used always the same colour for each protein. This was fundamental for Raff too who himself used colour as information to provide roughs (sketches) to Roberts.[441] In Martin Raff's view, colour had to be used in a very particular systematic and reliable way otherwise it could play against the production of a clear and sound visual message.[442] You cannot have for instance, the same protein having different colours in different illustrations, it would have been very confusing for students. Julian Lewis thinks similarly about the advantages of using colour, he remarked:

> It is more cheerful in full colour, […] it always reminds me when I was at primary school or before primary at kindergarten when we had these books on to learn to read as you went through the series they got to be more colourful, there was a special thrill to get the new book that had the full colour… anyway, I feel a little bit like that about this, colour, yes it gives a lot more of freedom to emphasise things, distinguish things than if it were in black and white. [443]

438 MRI 01.02.14.

439 MRI 01.01.55.

440 MRI 01.06.14.

441 MRI 01.04.50.

442 MRI 01.05.52.

443 JLI 00.21.34.

Another element that could have brought a setback for the latest visual form of molecular imagery as depicted by Roberts was a sort of revival that microscopy had in the early 1990s when a new type of fluorescent labelling methods began to be used in conjunction with a new type of optical microscopy. By the early 1990s when the green fluorescent protein (GFP) was cloned, a new family of fluorescent dyes was born and with it a modified form of microscopical imagery. GFP, which is produced by a green-fluorescent algae was cloned in 1992 and soon began to be used extensively as a 'visual tracer'.[444] Many labs around the world became to rely more and more on its use together with biochemical methods, such as Immunoprecipitation/Western blotting (IP/WB) in signal transduction studies, to indicate proteins interacting (the most prominent example of third-generation models of molecular imagey). The gene of GFP was placed together with the genes of a given protein of interest, and then co-expressed in a recipient cell where the localisation of that protein could be assessed under the optical microscope due to its co-expression with GFP. One of the main advantages of GFP use was to get rid of the unspecific staining given by the traditional process of using antibody-associated fluorochromes. Alongside this development a new version of optical microscope came along at the time, that of the confocal microscope. The confocal microscope allowed overcoming a significant problem of light microscopy that was always present but became more problematic as new fluorescent dyes developed. Confocal microscopy allows the removal of the entry of light peripheral to the main focus by focusing only on a single and very thin plane of the specimen. The fluorescent signal thus contains the specific light from the fluorochrome and not the spurious light from other fluorochomes and/or from secondary irradiation. The capacity to section (visually slicing) cells, as a result of the combined use of GFP and confocal microscopy also created the possibility of producing 3D type of images of them and with it more precisely define spaces of interactions between proteins.

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444 Douglas C Prasher. Virginia K Eckenrode. William W Ward. Frank G Prendegarst. Milton J Cormier. Primary structure of the Aequorea Victoria green-fluorescent protein, *Gene*. 1992, 1: 229-33.
See also: Martin Chalfie. Yuan Tu. Ghia Euskirchen. William W Ward. Douglas C Prasher. Green fluorescent protein as a marker for gene expression. *Science*, 1994, 263: 802-05.

With more laboratories increasing the use of both technologies the possibilities for microscopical imagery regaining a lost representational territory increased. Nevertheless, this revival of optical microscopy did not have any impact on the imagery used on MBC (almost no changes in the percentage of optical images over the total for the 1989 and 1994 editions, **(Graph 2,** see page 117**)**. Images of a GFP and confocal origin did not feature in the 1994 edition; GFP is not even mentioned in its index in spite of the widely use of that GFP began to have in the labs in around those times. This situation changed in the fourth edition of 2002 in which the number of images from the total obtained with light microscopes increased from 5.29% in the previous edition (1994) to 8.30% **(Graph 2,** see page 117**).** In Roberts's view the advent of GFP based confocal microscopy, although it created some problems, did not challenge or put under a significant threat the original 'illustration program'.[445] The challenge came because there was a big temptation, Roberts argued, 'to flood the book with the proliferation' of the improved and 'wonderful images of locations of proteins' that began to emerge. In his view it became very tempting to use the hundreds of GFP photographs that arose in scientific papers.[446] Prettiness however does not mean too much if it does not make a point, in other words, if it does not tell a story. Roberts expressed this with the following metaphor: 'The van Gogh picture is pretty, but it tells you a story, it shows you an alternative way of looking at the conceptual point that is made in the text'.[447] Clearly for Roberts the confocal images using GFP were more factual perhaps, but certainly not at the same level as a van Gogh. The difference between a van Gogh and a GFP image was that none of these fluorescent images managed to make a point. A similar situation happened with the huge rise in the number of images of protein structure itself, those created with computers and the aid of other technologies such as X-ray crystallography or nuclear magnetic resonance. For Roberts it was irrelevant to get excited about it and put in the book every single new protein that has been cloned and its structure described.

To anticipate an issue I will be dwelling on later, what began to challenge the illustration program rather than the resurgence of microscopical imagery was 'complexity', and this

445 KRI 00.59.48.

446 KRI 01.01.10.

447 KRI 01.01.25.

came from another from of expression of molecular imagery, that of its third-generation models.

### 3.2.11. Some reflections on creating images of the invisible and the importance of its relation with day-to-day objects: The continuity of vision argument.

One important question when creating images of the invisible is where from the invisible takes it forms? Is it based on completely new forms created out of nothing or is there any relation with forms that are known by the artist and transformed? How did Roberts create images of molecules? Concerning this issue Roberts gave an interesting and nuanced answer:

> It's interesting, I suppose I was… I was brought up partly and certainly by inclination as… I was an old fashioned left wing materialist I suppose and that sort of…. rightly or wrongly forces you to think about these things as things, as objects. If these things are objects the best way of making them appreciable is simply to draw them as objects… You can't draw an electron cloud, you can't draw uncertainty you can't… So, it is actually not very helpful […]. The other thing is you can't fudge in a picture…you can't… if you think it may be like this or it may be like that when you actually come to draw it you actually have to make a decision sitting at the drawing board you know you actually have to do it, one way or another and it has to be so, and that is also a quite a powerful driver to drawing things, making them real you can't sort of have this sort of… fuzzy edge or something… it's got to be a line…. [448]

Not surprisingly perhaps, it seems then that preconceiving the world as something material and tangible, as formed by particles, is essential to creating images of the invisible; something that, in Roberts' view, acts as a constraint to the always temptations of fudging and cheating.

448 KRI 01.19.05.

So, what would be the limits of Roberts' drawing technique, the limits to the free imagination, what is possible and what is not possible? When confronted with this question he answered:

> I will find it very hard to illustrate a sort of quantum physics book for example you know that thing…things like Feynman's diagrams, you know, I just… a stroke of genius graphically, they really are astonishingly, clever inventions, really creative thing and they are part of the science and I can't imagining drawing. I just don't have not the feeling for those sort of…. for quantum physics that sort of whole realm about uncertainty and indeterminacy and you know… I am still back in the world where atoms are like little billiard balls [?] that you can draw them and I think I am more comfortable on that world.[449]

From Roberts' words, it is clear how important it is finding a visual reference from our naked-eye sense experience when depicting invisible, as it was to Pauling and his colleagues when they developed the 3D models of proteins, with billiard balls.

'The safe cracker', an image of a 'protein assembly pattern' which serves to explain energy changes in substrates, the 'walking tooth', an image that serves to visually convey the idea of energy associated protein changing form **(Figure 27 A and B,** see page 167 respectively**)**, and other figures such as that where a human-like foot and hands forms are used to differentiate between two alternative molecular mechanisms for the final production of a messenger RNA (self-splicing of introns) **(Figure 27, C,** see page 167**)**, are images that build from familiar forms and themes we are all accustomed to. [450] This necessity to create images that relate to what is familiar to the naked-eye and Roberts's preoccupation and insistence with scaling things properly has clear connections with the continuity of vision argument (see discussion on Chapter 1).

Roberts gives an example of the importance of relating to what is visible to the naked-eye (as well to the reliance in a previous representation) when he wanted to convey

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449 KRI 01.20.46.

450 Alberts, et al. 2002, op. cit., pp. 326. Fig. 6-36.

the idea of how long the human genome is.[451] He decided to create an image that included a 'little map of the world (an image we are familiar with from geography) with a red line across the middle of Africa, that is where 'humans arose' to 'present' it.[452] So that if the bases were drawn 1mm apart (as the convention says it should be), then the human genome will be over two-thousand miles (3200km in the figure) and so be able to go round the middle of Africa.

The necessity of referring to the visible when drawing the invisible is confirmed somehow by the drawing of things for which it is difficult to get a visible referent, such as uncertain, un-material things that are in addition in motion. On this last Roberts thinks that:

> The other thing you can't draw it, that you can never get over in a book like ours is simply a product of the scale of what you are drawing. You draw something big that actually is small, and is very difficult to appreciate dynamics, you know, how fast…molecules really do move around and diffuse and encounter each other. It always seems amazing that you know, that a single enzyme can find a single substrate molecule in a cell that is ten microns across, […] actually to appreciate how fast things are moving is, is terribly difficult, and you can only do it by analogy I think, and that has to be in the words I don't think you can have easy visual equivalents for those sort of complicated events.[453]

Julian Lewis also has some relevant reflections on the process of depicting 'invisible entities'.

> Depiction of reality as depending on microscopes is one thing, but there are other ways of doing it, which I think is also valid and that is… there are some processes like DNA replication for example which you can't see under a microscope as it actually occurs, it is not an useful way, but you do know from biochemical studies rather precisely what is going on and there are some fabulous …movies made sort

451 Ibid. pp. 202. Fig. 4-16.

452 KRI 00.46.0.

453 KRI 01.21.47.

> of three-dimensional movies of DNA replication in particular by some people who got lots of money at Cold Spring Harbour to do just that' […] But those, that seems to me is a really wonderful extension of one's perception is strange, you know, is very different from conventional microscopy because is more constructive less passively looking, but it demands the same thing, and I think that having develop own intuition about things by images is very important. [454]

A couple of crucial issues emerge from Lewis' comments. Firstly, he implicitly distinguishes the two cultures of image production the microscopical and the molecular and sees the second, very likely building on the continuity of vision argument, as an extension of the first. In so doing, he unproblematically conflates all levels of 'observational instances' on cells (microscopical and molecular), in one, as if, on the one hand, the different technes were able to produce the same output (phenomena and appearance respectively), and on the other as if they relied in the same translational principles.[455] Secondly and more importantly, he recognises the constructed character of molecular imagery and the freedom of creative expression needed for its production, a condition that places them in a particular condition concerning experimental justification.[456]

Without being explicit, both Roberts and Lewis take the continuity of vision argument as an essential argument for the visual project of molecularisation as displayed in MBC.[457] It is interesting to notice that whereas in CB a clear distinction is made in between what the 'eyes' can see and what they cannot with an arrow dividing both

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454 JLI 00.24.20.

455 Observational instances are conceptualised as measurement instances by van Fraassen. See his discussion on appearances, as the result of theory dependent measurement outcomes, van Frassen, 2008, op. cit. Chapters 4, 5 and 6). van Fraassen opposes appearances to phenomena, which rather than being the result of measurement are the result of direct observation. Contrary to the position adopted in this study van Fraassen conceptualises microscopic images as the result of 'measurements', and as such as appearances.

456 See Chapter 4, subsection 4.5 *'Is there a context of justification for molecular imagery'*, for a discussion on molecular imagery and the context of justification.

457 For an explanation on the continuity of vision argument see Chapter 1, subsection 1.1.2: '*The expansion of microscopical imagery: The electron microscope'*.

domains **(Figure 28, A)**, MBC does not makes this distinction.[458] In it the capability of direct perception (vision) between naked-eye, and light microscope, between light microscope and electronic microscope, and so forth, is collapsed by the use of solid bars that overlap thoroughout different entities, organisms, cells, viruses, molecules and atoms (**Figure 28, B)**.

Up to the third edition of 1994 Roberts used only the image I just described to argue for the continuity of vision argument. In the 2002 edition another image was added with the aim of making even more explicit the continuity of vision argument **(Figure 16, B,** see page 77**)**. The image shows nine successive images, the first one of a human thumb and the last one of its 'constitutive atoms', linked in a succession.[459] It is in my view clear that even if in the legend of the image it is stated that this is an 'imaginary progression' the idea is so powerful that it effaces the claim and thus familiarises readers with the clear cut possibility to see at the atomic level. Moreover images like this are powerful devices that give confidence to trust the images as having a potential for the manipulation of molecules, one of the main targets of the molecularisation programme on life processes.

### 3.2.12. An 'Inspiring almost awe-inspiring' textbook. The receiving end: How MBC was reviewed in scientific journals. [460]

As Watson forecasted to Roberts when he invited him to participate in the production of a textbook on cells in 1974, MBC effectively, 'swept the field',[461] when it was finally published in 1983. Once out and despite having had an impressive process of feedback during its production the future of the book relied to some extent to what other colleagues would think of its qualities. MBC received many reviews in various journals

458 De Robertis, et al. 1980, op. cit., pp. 6. Fig 1-3 and Alberts, et al. 1994, op. cit., pp. 140. Fig 4.1.

459 Alberts, et al. 2002, op. cit., pp. 549. Fig 9-1.

460 F Vella, 1983, 'Molecular biology of the cell' (review), *Biochemical Education*, 11: 121-122.

461 Watson's original expression dated from a letter to Roberts dated July 2nd 1974, it reads 'I suspect the final product could sweep the field'.

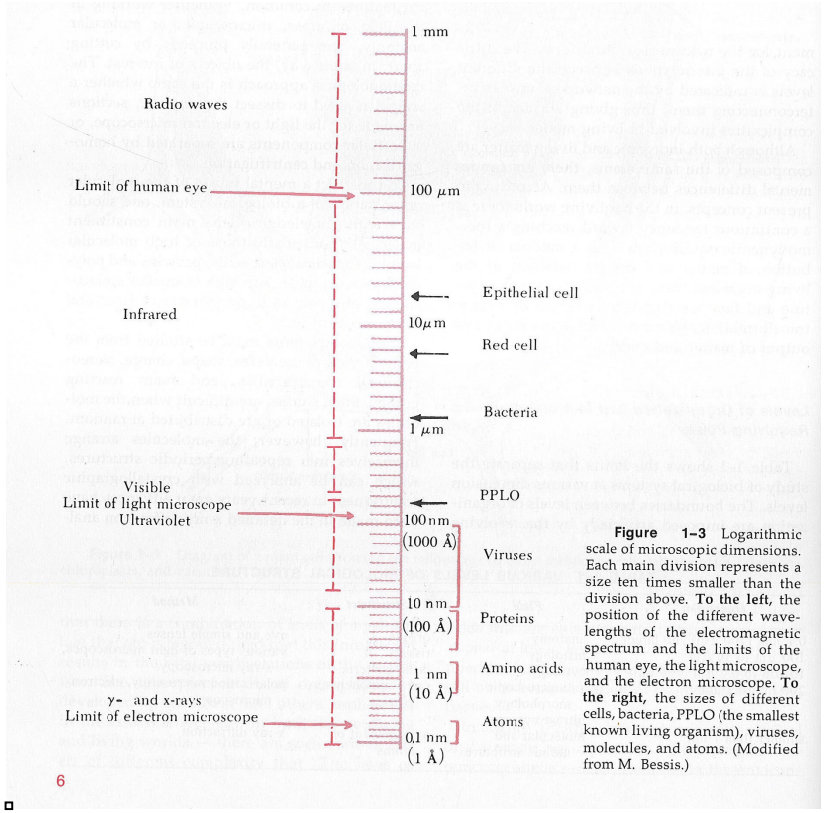


**Figure 1–3** Logarithmic scale of microscopic dimensions. Each main division represents a size ten times smaller than the division above. **To the left,** the position of the different wavelengths of the electromagnetic spectrum and the limits of the human eye, the light microscope, and the electron microscope. **To the right,** the sizes of different cells, bacteria, PPLO (the smallest known living organism), viruses, molecules, and atoms. (Modified from M. Bessis.)

**A**

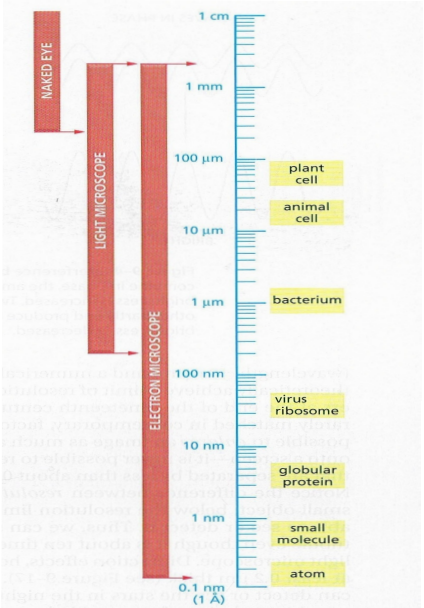


**Figure 9–2 Resolving power.** Sizes of cells and their components are drawn on a logarithmic scale, indicating the range of objects that can be readily resolved by the naked eye and in the light and electron microscopes. The following units of length are commonly employed in microscopy:
μm (micrometer) = $10^{-6}$ m
nm (nanometer) = $10^{-9}$ m
Å (Ångström unit) = $10^{-10}$ m

**B**

**Figure 28: The energy spectra in A) CB (1980) and B) MBC (2008)**

by scientists from different expertises and fields in the biosciences. Overwhelmingly they all considered it as a very up-to-date and well-presented textbook. As one reviewer put it when reviewing the second edition of 1989: 'the success or failure of a book hinges on how well it sells, how popular it becomes and how useful it is'.[462] The first edition of MBC was precisely that, a unanimous success on all fronts. The book passed with allure the acid test of the market economy of the 1980s and began to be a global product. It sold very well and went on to be rapidly adopted by most university courses on the UK, US, France, Spain, Italy, Germany and other countries around the world. The market research made by Burden and the painstaking work at universities gathering teachers and students feedback made by Miranda Robertson before and while the book was written had unquestionably and largely paid its fruits.

The reviews MBC received all contained high praise. One of the reviewers in the prestigious journal *Cell* described MBC as having 'top images', 'top writing' and as a book that was signposting 'the end of an era' and one that, 'gives a taste of what was to come'[463]. Although for the reviewer's taste MBC was quite close to Watson's previous MBG (he refers to its third edition, which was becoming more cellular), he considered that the book was a definite 'recipe for success' for the process of molecularisation of cell biology, one that he wished was around when he was 'trying to understand what genetics and biochemistry were really about 40 years ago'. MBC got another good review from a well-respected and longstanding figure in the field of classical molecular genetics, John Kendrew (1917-1997) from the Laboratory of Molecular Biology (LMB) in Cambridge. This in fact was one of the best things that could have happened to the authors of MBC. Kendrew labelled MBC as '*a tour de force*', as 'the text of the molecular revolution'[464]. He instantaneously recognised why the textbook was made and the role it would play in heralding a new era. He stated that: '[…] the molecular approach is making a 'takeover bid" for the classical field of histology, which had to depend largely on optical microscopy. The text of the molecular revolution in cell biology is splendidly presented

462 Martinez Areas Alfonso, 'Molecular biology of the cell', (review) *Trends in Genetics*, 1989, 5: 420.

463 Cairns John, Prospero's cell, *Cell*, 1983, 33: 1-2.

464 John C Kendrew, Essay review-The molecular biology of the cell, *Endeavour*, 1983, 7:4, 202.

in this book'. Kendrew also noticed the enormous labour put in by the authors into working out an outstanding imagery. He commented: '[…] The reader's task is made easy by the remarkably cleverly drawn diagrams that illuminate almost every page of the book, and this would be a key element in its success'. Kendrew was not the only one in noticing the importance of imagery for MBC in particular and for the development of a discipline in general. The images of MBC were described as a 'graphic design in pedagogy' by Joseph Gall a Professor of biology molecular biophysics and biochemistry from Yale University in his review of the book in *Nature.*[465] Besides, he regarded MBC as a textbook that had accomplished the challenge of putting all the growing information on cells and the different areas of biology, such as immunology, development and so forth, in one single treatise. Gall noticed the presence and effectiveness of the concepts headings in MBC. He also noticed one of the particularities of MBC, that of the large number of knowledge providers he stated in this regard: 'Much credit must go to the extensive reviews and contributions of some seventy five additional people listed in the acknowledgements'. However, the major credit, he argues, should go to the main authors', 'six experts' that just 'pool their talents' to produce an 'integrated and authoritative account'. Vella had also noticed the enormous number of 'hidden collaborators' that MBC had. He went further than Gall though by calling them an 'army of international helpers';[466] one that 'supplied material to be included in chapters, or that read them and criticized, and suggested amendments to parts or the whole of the nineteen chapters'.[467] Vella thought that MBC has everything to be a 'best-seller', that is, it had a good approach, a good content, a good presentation and a good price. What else do you want for a product to become a successful sell?[468]

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465 Joseph G Gall, Teaching mechanisms, *Nature*, 1983, 302: 637.x

466 Specialists on different subjects from the USA, UK, continental Europe, Australia and Canada.

467 Vella, 1983, op. cit.

468 I found two others reviews of the first edition from 1983 that I did not discuss for they are too short and do not add anything new to what it was just discussed from the reviews presented. They are: Gilmour Harris, 'Molecular biology of the cell' (review), Immunology Today, 1983, 4: 352. And that of HRV Arnstein, ' Molecular biology of the cell' (review) *Federation European of Biochemical Societies*, 1986, 196: 180-181.

There were a few exceptions to this overwhelming list of praising reviewers (some reviews in fact included both). One reviewer for instance, although recognising much intrinsic worth in the textbook such as 'the design and quality of the illustrations' and the clarity of its paragraphs and conclusions, deemed it, with a bit of irony perhaps, as a 'adventurous textbook in cell biology' (title of the review).[469] The title in fact, anticipated an important critique,[470] one that would re-emerge, as we will see above, on reviews of the further editions. Cairns seemed to be aware that many not fully confirmed 'facts' on cells became quickly incorporated as Roberts put it: 'as gospel in the book before' they were even published.[471] The author pointed out that the textbook made many generalisations and suggested many mechanisms for cells that were too speculative and not fully proven. This kind of critique would have sounded as bizarre to the 'old guard' cell biologists who in contrast to the new entrepreneurial type of bioscientists were not at all used to this kind of style. Theirs was extremely cautious and would almost certainly never include statements that were not fully proven by experimental outputs. Take as an example the following remark found in the prefaces of the 1948 and 1960 editions of the De Robertis et al textbook: 'Since many of the theories seeking to interpret cytological phenomena are still under discussion we have sought to avoid them as far as possible and to present the reader only with established facts'.[472] Critics viewing MBC as harbouring some sort of sloppy style would continue to appear in the reviews of the successive editions of MBC. In one of the strongest critiques I found the reviewer of the second edition (1989), viewed it as potentially confusing for new students for 'introducing complex material casually to illustrate a generalisation'.[473] The reviewer believed that

469 John B Gurdon, An adventurous textbook on cell biology, *Trends in Biochemical Sciences*. 1983, 8: 383-384.

470 The critique was also mentioned by Cairns, albeit in a softer manner when he argues that the readers are told about facts but not told where the facts come from. John Cairns, 'Prospero's cell', *Cell*, 1983, 33: 1-2.

471 KRI 01.08.15.

472 De Robertis, et al. 1948, 1960, op. cit. Arguably, this cautious attitude towards new not fully proved findings could explain cytology's lengthiness in the 1950s and 1960s to incorporate more rapidly the knowledge biochemistry or later molecular biology began to offer to the discipline.

473 AH Meheler, 'Books review: 'Molecular biology of the cell' and Molecular biology of the cell, the problem book'. *Biochemical Education*, 1990, 18: 51-52.

this ‘confusion’ was mainly created at the level of the images. Although recognising that the ‘illustrations are the mainly attraction of the book’, he objected to the use of the mixture of ‘allegorical elements to introduce the beginning student to (1) proteins (2) catalysis and (3) bioenergetics’, all topics that after him require familiarity with many component factors and that the book was not providing. ‘What inspiration is a beginning student to derive from’ showing a ‘snakelike mitochondria in an epithelial cell”, the author wondered. Joining into Cairns’s critique Mehler also thought that MBC presents fundamental information that is common knowledge to the authors, too prematurely. He further argues that although it is important for students to acquire mental images of the elements they are to use intellectually, ‘this should be as realistic as possible’ and ‘derived from properties established by scientific investigation’. Finally, he explicitly manifests his discontent with the methodological approach followed by MBC by affirming that ‘it is clear that as a biochemist I am not pleased by the treatment of my discipline’. This issue emerged again, with a more moderate tone though when the third edition (1989) of the book was out. In a review the author stated that ‘my only complaint about MBC is that it tends to treat many subjects a bit too superficially’.[474]

All in all, and despite the non-negligible level of criticsism raised at MBC the book was in the main viewed by reviewers as a good thing to happen to biologists, one that was as one of them put it, an ‘inspiring almost awe-inspiring’ textbook.[475] That MBC contained some speculative thinking and contained too ‘conceptual statements’, that made some careless generalisations or advanced issues as fact when they were not fully proven and finally that it was produced by far more than six authors, by an ‘army of internationals helpers’, as one reviewer put it were in fact many of the novelties that MBC brought about.

474 James P Trempe, ‘Clear molecular and cellular biology’. *Trends in Endocrinology and Metabolism*, 1995, 6: 10. He also equaled reading MBC with reading a novel. And pointed out that MBC not only served for upper level undergraduates students but to senior scientists too.

475 Vela, 1983, op. cit.

### 3.2.13. The case of signal transduction, its evolution through the editions of MBC and beyond. A source of its own success and of its own demise?

The particular kind of imagery that MBC brought about was one created by instruments and techniques that produce outputs of a non-visual nature. In fact, if there is a distinctive feature that characterises MBC over preceding textbooks in cell biology such as CB is the impressive development in it of the latest visual forms of molecular imagery. Without exaggeration signal transduction and the related membrane embedded receptors in contrast with protein trafficking, the theme that began to concern Porter, and 'old guard' cell biologist as he entered molecularisation, is a theme that belongs almost exclusively to the molecular culture and hence represents quite a disruption with past subjects of the discipline. A quick review of some numbers from the quantitative analysis on MBC will help us to grasp this **(Graph 2,** see page 117**).** The percentage of images from the third-generation models of molecular culture in the first edition of MBC (1983) represented a 10.45% of the total number of images that featured in the book **(Graph 2,** see page 117**)**, a significant value when compared with the 5.66% that, that kind of images represented in the 1980 edition of CB **(Graph 1,** see page 114**)**. What is more, this value would keep increasing through the successive editions reaching a 30.85% in the 2008 edition **(Graph 2,** see page 117**)**. The percentage of images obtained with the light microscope has kept increasing from 4.68% in the first edition (1983) to 8.22% in the 2008 edition, with a steady increase for the in-between editions**.** They are of an order of less magnitude to those in CB that have the values of 9.02% and 11.42% in the 1980 and 1987 editions respectively **(Graph 1,** see page 114**).** The percentage of images obtained with the electron microscope in MBC varies between 20.12% for the 1983 edition and 15.34% for the 2008 one with slight variation in between **(Graph 2,** see page 117**).** Overall, a close value to that of the 1987 edition of De Robertis et al, which was of 18.39% (its lowest) **(Compare Graph 2 and Graph 1,** see page 117 and 114 respectively**).** The data on **(Graph 2,** see page 117**)** allows us also to visualise which type of modelling process, cellular or molecular, is more relevant in MBC, especially when compared to the equivalent one for CB **(Graph 1,** see page 114**)**. In contrast to CB **(Graph 1,** see page 114**)** the percentage of the third-generation models from molecular culture largely supersedes the percentage of cellular or $e^-$ based models in all the editions of MBC **(Graph 2,** see page 117**)**. Lastly, the variation between the percentage of images

obtained with the electron microscope and the percentage of models based on those images **(Graph 2, $e^-$ based models,** see page 117**)** maintain a relation of correlation through the different editions of MBC as the one observed for the case of de Robertis et al **(Graph 1,** see page 114**).** This look at the figures from the quantitative analysis of the microscopical and molecular images in MBC supports my claim that the textbook acted as kind of embodiment of the molecular imagery in cell biology.

By looking historically at the discipline, it could fairly be said that signal transduction, is a 1980s subject and that as such marks a clear watershed in the history of cell biology, for it did not exist in classical cell biology treatises before MBC. [476] Signal transduction imagery however has a sort of independent development outside textbooks in scientific papers. In effect, a paper describing hormone receptors published in *Nature* in the 1980s displayed, albeit in a very simplistic way images.[477]

One important point to notice however is that the images of signal transduction pathways displayed in MBC were more in number, represented as depictions and more complex than those displayed in scientific papers (especially from the second edition of 1989). Many papers for instance, showed only the raw visual output of the instruments (bands in autoradiograms) rather than adventuring in creating images of interacting proteins. Moreover, compared to the others types of images of the third order, those of signal transduction are the ones that have shown a more sustained and important growth throughout the years inside and outside MBC. As anticipated in Chapter 1, signal transduction has shown from its first manifestation, a progressive development in the successive editions of MBC **(Figure 20,** see page 98**).** This development of this visual form of molecular imagery also found expressions in other media such as catalogues promoting the selling of bio-reagents for research **(Figure 21,** see page 99**)**, reaching a pinnacle of expression, with the publication of the interactome, a map of all possible

476 As mentioned in Chapter 1, the occurrence of term signal transduction in the scientific literature has increased from approximately 5 in the 1980s to 10.000 in the 2000s and by the year 2000, 12% of all papers that used the term 'cell' used simultaneously the term 'signal transduction'. Gomperts, et al. 2002, op. cit.

477 Martin Rodbell, 'The role of hormone receptors and GTP-regulatory proteins in membrane transduction'. *Nature*, 1980, 284: 17-22.

protein-protein interactions to occur in cells of the fruit fly *Drosophila melanogaster* in 2003 in the journal *Science* [478] **(Figure 22,** see page 101**)**.

Paradoxically, despite its success (in the view of its producers) as one of the most successful areas of cell biology, the development of signal transduction, one of the themes that have characterised MBC is becoming its own source of problems. In Raff's view the imagery of signal transduction is becoming out of control. On the making of the fifth edition he commented in this regard:

> As I read more and more of others authors' chapters towards the end now I begin to see that everything looks the same, you know, it doesn't matter where you are showing signalling or what it is that you are showing, but, they are all the same I mean these are signalling pathways and they are each different but for the bloody student they all more or less look the same and exactly the same thing is you are looking at trafficking, the way a cells work is proteins working in assemblies […] is all the same whether it be translation, transcription protein trafficking, a cell signalling. It doesn't matter what it is, the cells are doing the same darn thing, they are assembling their protein complexes, that they do their thing and then they disassemble and is all tightly regulated by five or six post-transcriptional modifications. But for the poor students every one of these things has a name every one and they are all different and they are meaningless. Is it important that they know the name of the thing?[479]

He considers that from now on (2007) the situation has reached an inflection point, one that clearly shows that from now on things have to be done differently.

The crisis for knowledge production on cell signalling derives from the degree of complexity the field has reached, for which its imagery is largely responsible. The complexity of signal transduction pathways began to say nothing about cells. In Raff's own words:

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478 Giot, L, et al. 'A protein interaction map of Drosophila Melanogaster' *Science*, 2003, 302: 1727-36.

479 MRI 01.20.26.

> Just to be able to know what the components are, which interacts with which doesn't tells you how the system works that's… you know, you can name every …and is the same thing with the brain you can know every neural cell, you can know every cell that connects with, you can know all the ion channels that mediate how the action potential works and still don't understand how the brain works.[480]

It is to some extent paradoxical that after so much investment in this kind of 'networking visuality and epistemology', according to Raff it is time (2007):

> […] To turn your mind away from these block models, because the block models are giving you a really fundamental misconception of how everything works. So, I think it's not unreasonable that we've gone through this era, you know when students thinks about a signalling pathway, they think about these blocks that is how they think it happens they think about these blocks, you know… one block is going to get together with another block, not that one thousand of these are interacting with another thousand of these'.[481] 'It's really a question to what extent is this symbolism of blocks which are drawing for the eye to see, which is a totally misrepresentation of what is actually happening, to what extent it is misleading and we know it's hugely misleading but what else can you do, is there an alternative?[482]

According to some of his colleagues the alternative would be to create 'massive connected diagrams that look like electronic circuits' and concomitantly to produce mathematical equations able to express for instance how tight or weak, hence how possible and important or not those interactions are. Raff does not think however that, this is the way things should move forward. In his view (although not proposing a clear

480 MRI 01.27.55.

481 MRI 01.39.13.

482 MRI 01.39.58. Notice the use of the word 'symbolism' by Raff to express this kind of imagery. Much in line with the way 'structural objectivity' considered it, that is, as potentially misleading.

alternative) he stated that: 'I think next is going to be in an even more simplified and misleading format, not longer even attempting of giving size'.[483]
When asked about the issue of the expanding imagery of signal transduction models Raff remarked: 'I think you put your hand on… your finger on into a critical next stage, you know, we know it's misleading but how can we teach it'.[484]

Viewed as an issue of overwhelming complexity the problem also seems to concern Roberts and Lewis. As Roberts put it: 'to illustrate processes where there are networks that are in more than two dimensions and where there are complicated feedback loops that simply becomes no longer really possible to draw in simple 2D form I think effectively'.[485] A view, which is also shared by Lewis who stated: 'What I am a little more hesitant about it is the attempt to give figures a sort of three dimensional character, […] even if the objects depicted may be three-dimensional like protein molecules for example we often do not know enough about that 3D structure'.[486] He thinks that to put it straightforwardly into a two-dimensional diagram is not only 'pretentious', but also only a 'decorative detail', almost a waste of time. Specifically on the consequences of the expansion of the imagery of signal transduction, Lewis commented: 'A lot of imagery on cell signalling, I think is very boring is just lots and lots of different coloured blobs interacting with one another'.[487] Lewis is keen to remark that this imagery of 'colored blobs interacting' is a 'very simple and naïve way of thinking about things' and that hence could be misleading.[488] In his view, 'without making measurements and making models you can be completely mistaken about where is the key site of regulation'.[489] Lewis thinks that because of this tradition of depicting molecules that way, that of

483 MRI 01.41.00.

484 MRI 01.42.01.

485 KRI 01.05.09.

486 JLI 00.22.30.

487 JLI 00.32.00.

488 He refers in particular to the action of a signalling protein known as transforming growth factor beta (TGF β) signal.

489 JLI 00.49.18.

coloured blobs interacting, ('the easiest way of presenting things'), we inherit a static picture, so that, 'there is a huge emphasis on those, but the reality is that these processes are occurring in time and timing is all important'. The imagery is missing the statistics, time and the spatiality.[490] There are turbulent times ahead for cell biology in Lewis view for two main approaches are confronting the validity of their results. On the one hand there is whole genome analysis and microarray technology, which is revealing a large number of molecules and a huge multiplicity of partners to interact with and on the other the traditional geneticists' work of identifying things according to phenotype, to things that, in their view, really matter.

As mentioned at the opening of this subsection it is somehow paradoxical that one of the avenues of research that gave MBC a lot of its visual character has become the source of its own defeat. In effect, the current state of signal transduction and related areas such as systems biology seems to be a determinant one, for the future existence of MBC or at least of how the book looks. In a Shakespearian tone the authors are currently (2009) debating MBC 'to be or not to be', in which direction to take the next edition of the book. If MBC is to remain the best representative of an easy understandable, at times misleading but beautiful cell biology textbook mainly for students, or if it is going to be a more mathematical based book exclusively written for professionals. On reflection, it is difficult to imagine MBC moving away from that highly conceptual, block biology, the one that to some extent they themselves and Roberts in particular created and that made of the book such a success among students. Why should MBC have a different fortune than other classics textbooks on cells as such as Wilson's or De Robertis', after all the passing of time and the disappearance of particular cultures of knowing and making images seems to be an inevitable process to which no textbook could escape.

An important issue to keep in the back of our minds as we move into the following chapter is that by harbouring the latest forms of molecular imagery MBC was to act as a visual catalogue for a 'new' kind of signs in cell biology.

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490 JLI 00.54.01.

## Chapter 4. How to read the visual change: The theoretical and historical locations of this study.

An issue that stands out from the previous chapters is how much in a period of 50 years (1950-2000) the visual landscape of cell biology textbooks has changed because of the input of molecular culture from the 1980s onwards. To conceptualise this visual change, as a progressive one, one where a form of representation, the microscopical, is substituted by a more sophisticated one the molecular, would be too simplistic.[491] This would also signify an unfair dismissal of an enormous body of scholarly work, from social and anthropological studies of science that have drawn attention to the complex and intertwined process of production of knowledge and images in science. A key aim of this study and this chapter in particular is thus to bring an alternative reading for the visual change to the received view that portrays this visual change as an inevitable path towards progress, with images defining better and better how cells 'really' are. A first necessary step in that direction is to show the limitations of the received view that portrays representational changes as progressive events. This first step is accomplished by discussing some previous theoretical works on issues of invisibility and ontology (Arabatzis, Cambrosio/Keating and Rheinberger); a discussion that will let us appreciate the difference between the microscopical and the molecular imagery at the level of the translation of visual outputs.[492] Semiotics is then introduced as an alternative reading of the visual change. Reading images as signs and exploring the connections between the different types of images that composed the visual landscape of cell biology will help us to understand not only the different qualities that the microscopical and the molecular imagery possess, but also to gain insights into how images of the latest forms of molecular imagery achieve their legitimacy to define cells. In view of a recent work by Daston and Galison, where the attainability of 'objectivity' is historicised an attempt is given to localise the microscopical and molecular imageries within this history.[493]

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491 This is the most common position taken by cell biologists. A slight variation is considering the latest form of representation as complementing the former one.

492 This exploration will allows us to move into some important features of the cultures involved in the production of both imageries (see Chapter 5).

493 Daston, 2007, op. cit.

Finally, the chapter ends with a discussion on the applicability of the 'context of justification' to molecular imagery.

Studies on issues of scientific representation and scientific imagery are the most appropriate ones for the theoretical framing of this study. This however has not been a straightforward task. The reasons for this are manifold. Firstly, the existent literature dealing with issues of 'representation',[494] and/or imagery in science and in particular in biology is vast.[495] Secondly, there is a great variety of approaches: sociological, philosophical, anthropological, cultural and artistic, used on their own and/or in combination to conceptualise the use and role of representations and images in science that reach different conclusions on the theme. The ways, say philosophers, sociologists or biologists conceptualise the concept of representation differ to a great extent. Whereas biologists, for example, more commonly conceptualise representations, of different origins such as drawings, charts and photographs, as mirror-like images of the real world, philosophers associate them more straightforwardly with models and theories. Thirdly, these different conceptualisations arise partly from the different meanings that the

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494 I use the word representation to refer to representations of a visual rather than a mental nature. Although they overlap in many respects one important difference between them is that things represented mentally are, (if not translated into a external depiction) thoughts. Conceptual abstract constructs without a material from such as 'market forces' or 'the unconscious', are clear mental representations (they can take a visual form if charted). Things are similarly controversial for other type of 'invisible' entities such as 'atoms' or 'molecules'. They are considered as 'visible' because they are taken to have a material form, hence a visual form for realists, but supposed to be 'hypothetical' (without a physical form), by instrumentalists or constructive empiricists.

495 The number of books and articles on the field is so immense that is simply impossible to list all the works here. The following ones give a good coverage of the different ideas on imagery and visual representation in science from different perspectives (artistic, philosophical, sociological etc: Nancy Cartwright, *How the laws of physics lie*, Oxford, Oxford Clarendon Press, 1983. Caroline A Jones & Peter Galison (eds), *Picturing science producing art*, London Routledge, 1998. Jan Golinski, *Making natural knowledge: Constructivism and the history of science*, Cambridge, Cambridge Univeristy press, 2005. Harry Robin, *The scientific image: From cave to computer*, New York, Oxford, England, W.H Freeman and Company, Publishers, 1992. Hacking, 1983, op. cit. Lynch, et al. 1990, op. cit. Arthur A Miller, *Insight of genius: Imagery and creativity in science and art*, Cambridge, Massachusetts, MIT Press), 1996. Brian S Baigrie, *Picturing Knowledge: Historical and philosophical problems concerning the use of art in science*. Toronto Buffalo, London, University of Toronto Press, 1996. Luc Pauwels, (ed.) *Visual cultures of science: Rethinking representational practices in knowledge building and science communication*, Hanover, London Darmouth College Press. University Press of New England, 2006. van Fraassen, 2008, op. cit. Martin Kemp, *Seen/unseen: Art, science and intuition from Leonardo to the hubble telescope*, Oxford, Oxford University Press, 2006. Martin Kemp, *Visualisations: The nature book of art and science*. Berkeley, Los Angeles California, The University of California, 2000. Some other relevant works are cited later in the chapter.

concept harbours, a situation that has a long history behind.[496] From the fifth century BC times in Greece through the 15th- to 17th century European Renaissance to the present there has been an ongoing critical debate on how mimetic representations are and/or should be. This long running discussion is about how much degree of resemblance (imitation) an image, which is supposed to 'represent' is allowed to have. The relevance for this study to this ongoing debate therefore resides in the possibility to explore where the microscopical and the molecular imagery are located inside this assumed gradient. This is a central issue for this dissertation, an issue to which we will come back in more depth once we have introduced semiotics as an alternative structure to read the visual change undergone by cell biology.[497]

Before moving to the main topics of this chapter there is a point that requires clarification, namely: what this study is not doing.[498] This study is not about models. It is instead on the images that contain them.[499] As we have seen in the two previous chapters,

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496 Arguments on the complexity of the concept of representation and a call for its review have been claimed by Michael Lynch's article 'Representation is overrated: Some critical remarks about the use of the concept of representation in science studies', *Configurations*, 1994, 2: 137-49. Aware of the imprecision of the use of the term 'representation' Lynch pleaded for an open re-examination of its use. He argues that science studies have revealed that the concept of scientific representation gets conflated because of the heterogeneity of its meaning. The concept of representation thus is used indistinguishably to refer to different types of image such as a picture, a drawing, a chart or a photograph, all of them with a different epistemic content.

497 See the forthcoming subsection *'Representation and microscopical and molecular imageries the lessons from semiotics'*.

498 The only time this study touches upon models is in Chapter 6, when it considers the neglect of the cellular model.

499 The literature on models is as vast and varied as that on 'representation'. A few are given in what follows. One line of thought for instance takes models as mediators between reality and the theoretical assumptions about that reality. See Morgan, et al. 1999, op. cit. For a critique of Morgan and Morrison work see the idea of models 'of' events and simultaneously models 'for' the production of new experiments developed by Keller, 2000, op. cit. Visual representation, quite often overlaps with the term 'representation' as understood in philosophy, which encompasses the activities of modelling and theorising. For the different view of models from scientists and philosophers and the process of production of scientific imagery see Michael Lynch, 'The production of scientific images: Vision and re-Vision in the history, philosophy and sociology of science'. *Communication & Cognition*. 1998 31. 2/3: 213-228. From the role of models as representational devices from a philosophical viewpoint see: Ronald N Giere, 'How models are used to represent reality', *Philosophy of Science*. 2004, 71: 742-52. And Mauricio Suarez, 'Scientific representation: Against similarity and isomorphism'. *International Studies in the Philosophy of Science*, 2003,.17: 225-44. For the importance of 3D models on the creation of knowledge in science see de Chadarevian, et al. 2004, op. cit. For more recent developments see Roman Frigg, 'Models and fiction', *Synthese*, 2010, 172: 251-58. A study that could understandably be perceived as provocative for some philosophers and scientists alike, for it, is based on the work of Kendall Walton (1990), equates scientific

most of the images of molecular culture present in CB and especially those of the third-generation in MBC are strictly speaking models.[500] That said, and however important models are for the production of knowledge in cell biology, this study prioritises the value of images in itself regardless of the models they contain.[501] This selective move has a reason. Models are first of all images and as such they contain an extra meaning and an extra epistemic function that arises precisely from their condition of being images. As discussed later in this chapter, based upon visual and cultural semiotics, images/visual representations are signs and as such they function at a different level from that of models as a meaning-making system, especially in what concerns the attainability of legitimate knowledge.

Despite the above-mentioned existence of diverse approaches that on their own or in combination engaged with issues of representation and or image production in science, they all coincide on some crucial points. Firstly, on the pivotal role of representations for the production of knowledge in the sciences,[502] all studies basically agree that without representation there is no scientific knowledge. Secondly, they all portray representations and visualisations as simultaneous processes and products that make the epistemic objects of science observable, operable and intelligible.[503] Another theme that many of these studies have in common is a disregard for the difference between what can be seen with the naked-eye and what cannot (see later discussion of Rheinberger's 'epistemic things' for instance). One obvious consequence of this position of conflation between the visible and the invisible is the concealing of the different ontological qualities of what is being represented in our case, cells or molecules. Although not the main focus of this study it is important to keep in the back of our minds the following. The visibility and

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models with some forms of literary fiction. Kendall L Walton, *Mimesis as make believe: On the foundations of the representational arts*, Cambridge, MA, Harvard University Press, 1990.

500 Images of signal transduction for instance contains a model which is a hypothesis, proposal or theory about a cell mechanism.

501 Of course that does not means a neglect in my work of the role function and characteristics of models.

502 Pauwels, op. cit., pp. vii. Rheinberger, 1997, op. cit. Harry Robin, *The scientific image: From cave to computer*. New York, London W.H. Freeman and Company Publishers, 1992.

503 Rheinberger, 1997 op. cit.

invisibility of an object is not straightforwardly related to existence (ontological status). An image may refer to objects that have material existence or mental constructs of inmaterial 'assumed' entities.[504] The referent then could vary from a material to a mental construction. Equally, material or non-material objects having or not visual features could, after a process of translation, be transformed in a visual image. For the case of microscopical and molecular imageries important differences at the level of translation between the produced image and its referent (cell) are at play.

Critical contributions that have helped to clarify the concealed relationships between an image (a representation) and its referent and between visible/invisible objects and/or phenomena on one side and their ontology on the other are those belonging to the field of anthropological studies and/or social studies of science.

By focusing on the actual laboratory practices these studies have shed some light on the complexity of the process of image making and on the relationship established between representation and referent. Although not in a strict sense an anthropological study this one shares with them many of their aims and conclusions. A classic example of this kind of study is that of Latour and Woolgar, one of the first anthropological approaches that targeted a contemporary laboratory and showed the practices that turn scientific objects and events visible and accountable.[505] The other classical approach is that of Knorr-Cetina whose work has highlighted the complex process of negotiation and differential interpretation of scientific results (including visuals) and allowed insightful conclusions on the rooted nature of scientific knowledge in culture.[506]

Regardless of the degree of agreement one may have with the conclusions reached by these and other related studies they stand unquestionably as highly inspirational.

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504 Luc Pauwels, 'A theoretical framework for assessing visual representational practices in knowledge building and science communication', in L Pauwels (ed.), *Visual cultures of science: Rethinking representational practices in knowledge building and science communication'* Hannover, London, Darmouth College Press, University Press of New England, 2006, pp. 2-4.

505 Bruno Latour, Steve Woolgar, *Laboratory life: The construction of scientific facts*, Princeton, Princeton University Press, 1986.

506 Karin Knorr-Cetina, *The manufacture of knowledge: An essay on the constructivist and contextual nature of science*, Oxford Pergamon Press, 1981. Knorr-Cetina, et al. 1990, op. cit.

Much in line with Hacking's proposals in his classic, *Representing and Intervening* (1983), anthropological studies have helped to move the concept of representation away from theory towards the practices involved in its production.[507] By doing so, the conclusion of these studies has bounced back on the issue of theory-making and created a richer, and more comprehensive picture of it, one showing that 'representing and intervening' rather than being irreconcilable are the two sides of the same coin. Moreover, one of the main consequences (contributions) of anthropological and science studies, by looking at science in its making, is to have exposed many activities in the practice of science, such as the ones discussed in Chapter 3 on the production of MBC, that would otherwise remain concealed to external viewers and taken for granted by its practitioners.

One of the most prominent findings of anthropological studies has been the description of the transformation of research objects into 'inscriptions', that is, pictorials and text of a new type able to act as proxies for other non-present entities. How once created those 'inscriptions' become transformed into quasi objects, and begin to circulate to other places, such as labs, seminars, public displays, etc, ('immutable mobiles'), places where they are consumed, transformed and sometimes even re-invented.[508] All the images we have seen in previous chapters contained in cell biology textbooks could be considered to be 'immutable mobiles', which as Rheinberger put it, 'are characterised, not by what they depict, but how they work'.[509] By making the functioning of laboratory practices visible to wider audiences the analysis of visual representation has, if not given some answers to old questions, given at least, the opportunity to view them from a different perspective.

In a nutshell science and anthropological studies as a whole have shown that although important it is not only epistemological aims that produce scientific knowledge.

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507 Hacking, 1983, op. cit. This relation of representing and making is an important relation in my work. It will become more evident as I discuss the construction of indexicality in cell biology (see forthcoming subsection 4.3.3).

508 Bruno Latour, 'Visualisation and cognition: Thinking with eyes and hands', *Knowledge and Society: Studies in the sociology of culture past and present*, 1986, 6: 1-40. See also Lynch, 1998, op. cit., pp. 216.

509 Rheinberger, 1997, op. cit.

Besides, it is undeniable that anthropological studies have delivered some answers and that one among them is that images, are more than just auxiliaries to knowledge, that images do not operate outside discourse, and above all that the production of images in science is part of a complex process of creation, selection, negotiation and consumption among many participants, a process that as a whole remains black-boxed partially to its participants and almost totally to outsiders.

### 4.1. Invisibility and translations: Some key cases studies.

One way of understanding the limitations of the view that takes all latest forms of representation as more progressive than former ones, is by discussing important works that have dealt with issues of invisibility and that by so doing, have highlighted the complex process of imagery translation at play in those processes. (processes that for the case of cell biology were hinted at in Chapter 1).

Theodore Arabatzis' book on electrons is of particular relevance here.[510] By the end of the 19th century, electrons, Arabatzis argues, inhabited the world of both classical mechanics and electromagnetic theory. Soon after, because of their inability to explain certain phenomena, such as black body radiation, the speed of light and spectra emissions these two worldviews entered into crisis.[511] With the emergence of quantum mechanics offering an explanation for these two phenomena, electrons came to inhabit a new and different epistemic scenario.[512] Instead of 'being a point particle with a certain mass and charge' it became a mobile entity able to move between discrete orbits able to emit energy.[513] As we learnt from our discussion from previous chapters cells went through a similar process as electrons. While the microscopical image enjoyed exclusivity to represent cells well until the late 1970s, from that time onwards without fully

510 Arabatzis, 2006, op. cit.

511 Richard Dewitt, *Worldviews: An introduction to the history and philosophy of science*, Oxford UK, Victoria Australia, Blackwell publishing, 2004, pp. 192-99.

512 Arabatzis, 2006, op. cit., pp. 115.

513 Ibid. pp. 143.

disappearing it began to be superseded in number by molecular images of second and especially by those of third order.[514]

Historically speaking due to their minute size, electrons, even more than cells, have been very elusive entities, in Arabatzis's view, because under different experimental conditions they have displayed different features, a characteristic that has also made them resistant to association with particular theories. The creation of an image for the electron was related to the different solutions the physical and the chemical cultures envisaged to explain different phenomena. While the chemists wanted to explain chemical combination, physicists wanted to know about the role of electrons in the phenomena of atomic spectra and cathode rays.[515] Two contrasting images of the electron thus ensued. The chemists viewed the electron as a static particle, able to explain chemical bonds between atoms while the physicists viewed it as a very dynamic one orbiting at high speed around the nucleus. These two 'visions' of electrons, which belonged to two different cultures of thought (see later Chapter 5 for cultures of thought in cell biology), remained quite isolated from each other as if they belonged to two different paradigms.

Another central idea stemming from Arabatzis's work with similarities to the historical use of different types of imagery in cell biology is that the different 'representations' of electrons 'emerged from several problem situations', which ranged from chemical phenomena like electrolysis to physical types like the discharge of electricity in gases.[516] As we saw previously (hinted in Chapter 1) the 'problem situation' for microscopical and molecular imagery were quite different.

There is an extra relevant conclusion to be drawn from Arabatzis book: He argues for treating visible and invisible entities (observable and unobservable for him) differentially mainly because of the impossibility of direct physical access to them. Not

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514 See the classification of molecular imagery in Chapter 1, subsection 1.2.3: *The third-generation models: The visual forms of the third wave of molecularisation of cell biology (1970s to the present), from signal transduction to interactomes)*.

515 Arabatzis, 2006, op. cit., pp. 14 and pp. 190.

516 Ibid. pp. 109.

only that, as history shows, measuring an unobservable has in fact been quite troublesome but, 'paradoxically as it sounds the measurement associated with an unobservable entity does not imply that that entity exists'.[517] We have only to remind ourselves, he further adds, that the concept of measurement is 'laden with a realist presupposition'.[518] As my intention is not to reach a full conclusion about the existence/non-existence of invisible entities in general and in a cellular process such as that of signal transduction in particular, it suffices to insist only on the importance of treating them as different to visible ones and to assume an agnostic position concerning their ontology, a position which is close to van Fraassen's constructive empiricism and the position that Arabatzis seems to take in his book.[519] Arabatzis argues that the validity of his 'biographical narrative', endorsing ontological agnosticism resides in that it refers to 'representations of electrons' rather than 'the electron qua entity in nature'.[520] Arabatzis mid-ground strategy based on agnosticism, not to upset realist and non-realists alike regarding the existence of the electron is contentious but due to the complexity of the issue, a very respectable one.[521]

Arabatzis raises an important point concerning the problem of accessibility to the referent when he states: 'When it comes to unobservable entities, the claim that descriptions are used referentially cannot easily maintained, because it is not clear in what sense a description of an unobservable entity "picks out" that entity'.[522] This comment on the impossibility of access to the referent for representation of invisible entities will be of extreme importance for the forthcoming discussion in this chapter on the use of semiotics to make sense of the visual change in cell biology.

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517 Ibid. pp. 56 and pp. 62.

518 Ibid.

519 Constructive empiricism is the position developed by van-Fraassen in his book. Bas van-Fraassen, *The scientific image*, Oxford University Press, 1980. Basically this position takes a neutral stance concerning the ontology of the unobservable despite the fact of having epistemic access to those entities through observational albeit indirect (experimental data).

520 Arabtzis, 2006, op. cit., pp. 261.

521 Ibid.

522 Arabatzis, 2006, op. cit., pp. 258.

We now turn our attention to an illuminating article on the production of images of the invisible in cell biology by Antonio Cambrosio and Peter Keating.[523] Cambrosio and Keating's analysis is about the deployment of a new technique in immunology, one that produces visual images of a different nature to that of microscopes. This work is important because it is based, like the images of molecular nature described in this study, on the translation of one kind of output image into another of a different nature (see Chapter 1). The technique in use, known as 'cytometric imagery' is a technique for the visualisation of blood lymphocytes using means other than just the traditional fluorescent optical microscopy. The technique was originally developed around the 1970's to accelerate the counting of the number of lymphocyte cells with a particular phenotype out of a mixed population of white cells. Some years later the technique began to be applied to isolate morphologically distinctive lymphocytes from that mixed population of white cells with the aim of using them to evaluate the effect of certain drugs in 'pure' populations. The gadget that does the trick is known as a flow cytometer or Fluorescence Activated Cell Sorter (FACS) machine.[524] The sorting process is based on the functional differences between different cell types, which corresponds with a different molecular composition (proteins) in their membranes (phenotypic molecular expression). These distinctive molecules are targeted by specific monoclonal antibodies directed against them, which in turn are linked to fluorescent markers. A flow cytometer is able to recognise, count and eventually sort out with the aid of a laser beam fluorescent tagged cells from those which are not or from those cells labelled with a different fluorescent dye.[525] The flow cytometer takes measurements of the number of cells, manipulates them with the aid of a complex software to subsequently translate these 'raw' data into optical events, a plot image, on a computer **(Figure 29)**.[526]

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523 Cambrosio, et al. 2000, op. cit.

524 Ibid. pp. 236.

525 FACS machines were massively sold to immunology laboratories around the world and the growth in sales was paralleled by a growth on scientific publications involving the FACS machine, from 150 articles a year in 1980 to almost 3000 in 1992.

526 In their own words: 'A flow cytometer does not 'see'': it takes measurements that are subsequently translated into optical events in a computer screen' Cambrosio, et al. 2000, op. cit., pp. 239.

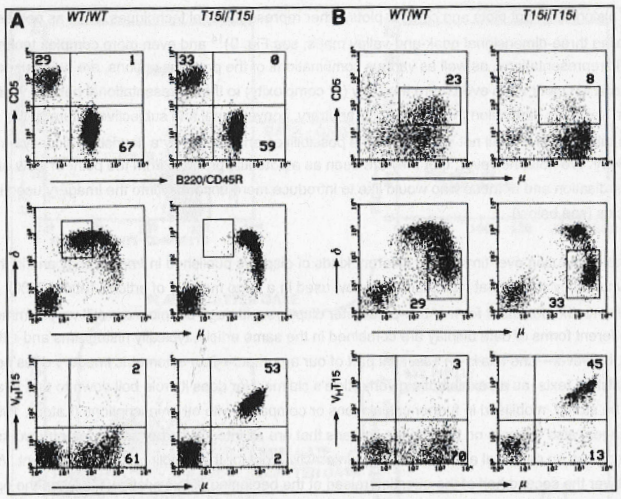


Fig. 3. Flow cytometric dot plots. The figure also illustrates the use of cursors and parallelograms to select (or 'gate') cell populations. Source: unpublished illustration kindly provided by Dr. Karl Rajewsky, Institute of Genetics, University of Köln (Germany).

A

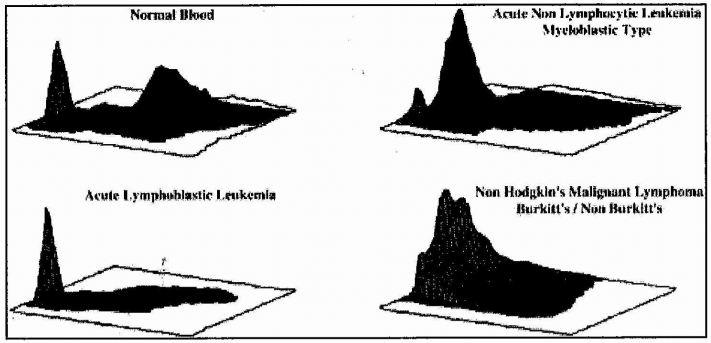


Fig. 9. Perspective plots as icons of normal and pathological conditions. Source: Immunopath advertisement, n.d.; original in colour. Reprinted by permission of Immunopath, Oncology and Immunology Laboratories, 7300 West 20th Avenue, Hialeah, Florida 33010, U.S.A.

B

**Figure 29: FACS dot plots and perspective plots of normal and pathological conditions. (A and B respectively) From Cambrosio and Keating 2000**

One of the main features arising from Cambrosio and Keating's study, which has many of the characteristics of typical anthropological studies, is the complexity of the process of production and consumption of images that would otherwise remain black-boxed.[527] At the level of production and adaptation of the FACS machine a complex series of 'translational' steps are required to get the final digitalised image of a 'cell population'. These steps involve an active relationship between the operator and the appropriated software to select the 'right' parameters for the sorting of cells ('gatting'), alongside the statistical calculations and multi-steps adjustment which are performed by the software of the FACS machine to finally give rise to a particular set of images, 'dot plots' which are then visualised in a computer screen. Cambrosio and Keating equate the flow cytometer as a 'sociotechnical device that because of its software, is situated in a spectrum of human and non-human agency'. This last point is an analytic concept belonging to the 'social network theory' programme, which grants agency to apparatuses and, as Cambrosio and Keating remind us, was originally developed by Latour (1987) and Callon (1986).[528] Similarly, they employ the concept of 'virtual witnessing', first developed by Shapin and Shaffer (1985).[529] This concept enables them to explain the 'collective disciplining' of the scientific community in the use and acceptance of FACS images. The concept of virtual witnessing also served them to explain the process of dissemination outside the sites of production of the scientific claims derived from the FACS experiments contained in the papers, a process that as we saw in Chapter 3 was also at stake, albeit in a different form, on the production of images for MBC. Apart from highlighting some of the complexities of the process of translation taking place during the detection of cells to the creation of images of 'cell populations', the authors made another bold claim. They argue that the new imagery brought about by flow cytometry embodies a particular approach to immunology (phenotypic expression); since what the new

527 Bruno Latour, *Science in action: How to follow scientists and engineers through society*. Cambridge Massachusetts Harvard University Press, 1987.

528 Bruno Latour, Michael Callon, 'Some elements of the sociology of translation: Domestication of the scallops and the fishermen', in J Law, J (ed.) '*Power Action and Belief: A New Sociology of Knowledge?* (London Routledge and Kegan, 1986.

529 Shapin, et al. 1985, op. cit. In fact the imagery resulting from experiments is only rendered possible through this disciplinary process of virtual witnessing.

imagery portrays is not cell populations *per se*, but cell populations as defined by another technology that of monoclonal antibodies.[530] This claim relates to the case of imagery in cell biology that as a discipline in the early 1980s started to embody the values and methodology of the growing recombinant DNA technology and other associated technologies such as monoclonal antibodies.

Despite its relevance I have a couple of reservations about Cambrosio and Keating's arguments. Firstly, although they distinguish two different meanings for 'representation', one to denote description and the other to denote theory they use the term 'representing' loosely, as if a representation of cell populations were transparently attainable (see the later discussion on mimetic and non mimetic representations).[531] Secondly, they label the digitally produced plots of cell populations in particular 'perspective plots' as icons of human health.[532] Plots as those displayed in **Figure 29, B**, (see page 205), are associated to connote different states of health or illness, depending on their differential pattern. These plots look more like symbols rather than icons, for they do not possess any relationship of resemblance to the 'real cells' (referent/object) as they look under an optical microscope.[533] Thus, in the case of plots, their association with a particular pathology is mere convention. In spite of these objections, Cambrosio and Keating's paper constitutes an instructive introduction to the large and complex multi-step process of translation involved in the creation of images of biological events that involves invisibles.

Another relevant work on the translation processes at work during the transformation of visual outputs of one nature into another is that of ethnographers of science Knorr-Cetina and Amann.[534] This work is key for my study because on the one

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530 Cambrosio, et al. 2000, op. cit., pp. 248.

531 Ibid. pp. 235.

532 Ibid. pp. 263.

533 See the discussion on the differences between icons and symbols in the following subsection *'An alternative way to read the visual change: Reading images as signs'*

534 Knorr-Cetina, et al. 1990, op. cit.

hand it focuses on the same kind of techniques at the basis of the images of third-generation models of molecular culture involved in the visual change that cell biology began to undergo from the 1980s (see Chapter 1), and on the other, because the authors provide a very useful terminology. Knorr-Cetina and Amann set out to explore the role of images as a topic and a resource in laboratory practice by focusing on a particular type of image known as the autoradiograph **(Figure 30)**. An autoradiograph is the imprint on X-ray film of the presence of radioactively labelled molecules such as DNA, RNA or proteins in the form of marks or bands (technique visual output).[535] As we anticipated in Chapter 1 when discussing the production of images of third-generation models of molecular culture, such as those of signal transduction, the image in the autoradiograph constitutes a particular visual output that is then translated in another type of visual output and/or image **(Figure 23,** see page 102**)**.

Knorr-Cetina and Amann's argument runs as follows: The autoradiogram is 'the result of an imaging technology that creates visible traces (bands) of invisible reactions'. Scientists analysing auto-radiographic images ascribe meaning to bands by talking in a particular way. Bands are taken as signs of the molecules (objects) by formal conversational routines, verbal exchanges that create a 'visual/experiential script'. This last, the authors argue, is made of a combination of visual and experimental knowledge; 'scenes in mind and pictures on file' derived from laboratory activities, disciplinary exchange and education that constructs processes and events for the referent.[536] The autoradiograph display is created, Knorr-Cetina and Amann argue, by five different domains or environments: a) The domain of embodied laboratory practices, b) the domain of invisible experimental reactions and events, c) the domain of publication, d) the domain of reference scenarios or precedent cases, and e) the domain of the image itself.[537] Although all-important factors, the domain of invisible experimental reactions

535 Molecules are labelled directly by incorporating radioactive atoms during their synthesis (DNA, RNA) or by using labelled agents or signal emitting agents that interact with them (antibodies) in a matrix such as nylon after being transferred from a gel (Western blotting) in which the proteins have been separated from each other according to their molecular weight (SDS- PAGE Electrophoresis).

536 Knorr-Cetina, et al. 1990, op. cit., pp. 263.

537 Knorr-Cetina, et al. 1990, op. cit., pp. 264-5.

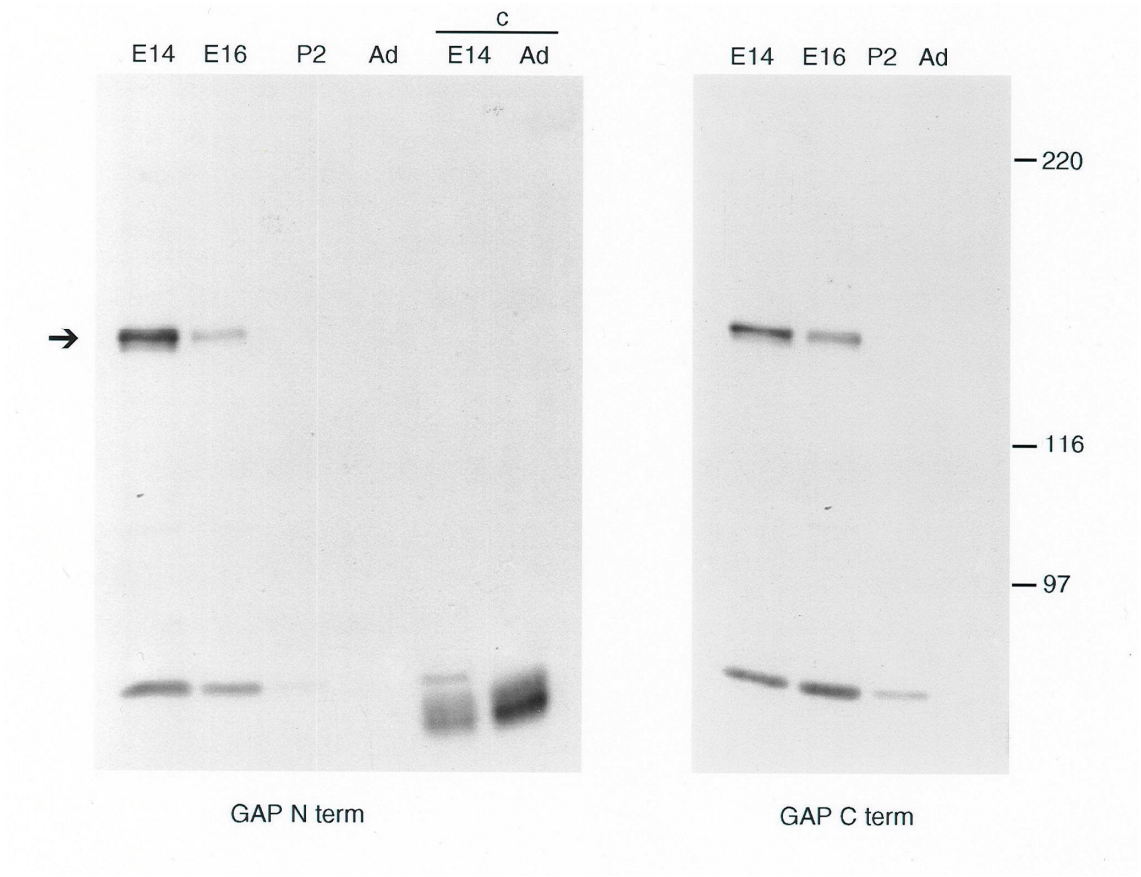


**Figure 30: Autoradiogram from an Immunoprecipitation/Western blotting experiment. Serpente et al. 1996**

and events is the one with particular relevance for this study, for this is the domain from which a large part of the extensive proliferation of images of a molecular nature in cell biology arose by the early 1980s.

The findings of this study support Knorr-Cetina and Amann's thesis that the autoradiogram constitutes a window into the realm of the invisible, a place where the traces of molecules and their interactions can be found. These traces or interactions are envisaged (and related to) through a language of design, language, which is in itself visual. The visual formulations asserted in this language of design are the object of discussions on invisible processes among scientists.[538] This process of transference in orders of visibility that the authors dub 'filling the test tube' is a result of three interacting systems, the bands on the autoradiogram, the visual formulation of envisaged interactions and the embodied laboratory processes.[539] By 'filling the test tube' scientists quite often look at former autoradiograms as referents for further talks, resulting in a situation in where, as the authors put it, 'many images are internally related by being predecessors or successors of others'.[540] This comment goes much along the lines of one of the main arguments of this dissertation, namely that the images of third-generation models of molecular imagery have become self-referential (see the full discussion on the issue in Chapter 6).

## 4.2. Rheinberger's epistemic things and spaces of representation: From traces to symbolic order.

Hans-Jörg Rheinberger's paper 'From Microsomes to Ribosomes: "Strategies" of "Representation"' (1995) constitutes a primer of an innovative and bold body of knowledge in scientific representation that he later published in book format with the

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538 Ibid. pp. 268.

539 Ibid. pp. 277-279.

540 Ibid. pp. 281. I will refer to this in Chapter 7 as the map/territory relation.

title: *Towards a History of Epistemic Things* (1997).[541] Rheinberger's approach is revealing for my studies because it provides a very elaborated terminology to analyse the growth of molecular visuality in cell biology from the early 1980s. Although the author uses a science studies approach to look at the representational practices developed in a laboratory between 1945 and 1965 in its first attempts to synthesise proteins in vitro, his conclusions are rather of a philosophical nature. One of Rheinberger's general aims was to answer the question of how 'novelty' in the form of objects is produced in bioscience by a process that is allegedly based on empirical rules. Two questions of a more defined philosophical nature are also at stake in Rheinberger's work, and these are: 'Is 'representation' just a manner of rendering the invisible visible, something hidden but ready to be disclosed? […], or is it a manner of translation, which literally means converting signs, traces in other traces, concatenating transformations?'[542] A key term that Rheinberger's uses in attempting to answer those questions is that of 'epistemic things', which refers to those new objects manufactured in laboratories as the result of experimental practices, that is, research objects as varied as physical structures, biochemical reactions and biological functions.[543] Epistemic things can be viewed as 'traces' that originate in a particular experimental system within a particular 'space of representation' where they mutually engender each other.[544] This last is another key concept that Rheinberger uses in his work. Spaces of representation refer to a conceptual space where 'epistemic things', like proteins, acquire material presence and a transient stability,[545] and the spaces where 'experimental systems display their dynamics'.[546] In his view, science viewed from a semiotic perspective is a symbolic system with epistemic

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541 Rheinberger, 1995, op. cit . Rheinberger, 1997, op. cit.

542 Rheinberger, 1997, op. cit., pp. 102.

543 Ibid. pp. 28. Rheinberger is keen to point out that one of the main characteristics of 'epistemic things' is their vagueness, this understood as them having a 'precarious status'; this because they embody as potential, what is not known about them (Ibid). The way I myself see this is that epistemic things are always in a state of tension between being and not being.

544 Ibid. pp. 105 and 110.

545 Rheinberger, 1995, op. cit., pp. 52.

546 Rheinberger, 1997, op. cit., pp. 224.

things interacting in particular 'spaces of representation'.[547] Spaces of representation are the product of several techniques old and new, techniques that, as those involved in the visual change that this study analyses, do not necessarily produce visual outputs *per se*. Thus, differential centrifugation, a technique that does not produce visual outputs in itself, participated together with the electron microscope, Rheinberger claims, in the creation of a particular 'space of representation', namely the 'particulated composition of the cytoplasm'.[548] Another important term used by Rheinberger is that of 'graphemes', which he defines as all the material traces, inscriptions, also including tables and diagrams, that derive from instruments that do not produce visual images, as for example, an optical microscope does. A graphematic articulation, that is the combination of the outputs from different instruments, constitutes the material form that epistemic things take when under investigation.[549] The traces left in an autoradiogram after a Western blotting experiment, one of the techniques at the base of the visual change in cell biology,[550] (see Chapter 1), for example, could be considered a 'graphematic' display.[551] An important conclusion that Rheinberger reaches is that the 'representations' resultant from different graphemes can be compared only among themselves but never against 'the real'.[552] This last conclusion is much in line with the one arrived at in this study that in modern cell biology the 'real cell' as created by molecular imagery is a representational space made out of traces. I agree with Rheinberger, that representation 'is the condition of the possibility' for things to become 'epistemic things'.[553]

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547 Ibid. pp. 104-5. As we will se in what follows he never fully commit to this position, for he thinks 'epistemic things' are material entities.

548 Rheinberger, 1995, op. cit., pp. 59-60.

549 Rheinberger, 1997, op. cit., pp. 106-7.

550 This biochemical/immunological technique together with another known as immunoprecipitation is the main technique at the basis of the field of signal transduction.

551 Rheinberger, 1997, op. cit., pp. 111.

552 Ibid. pp. 111.

553 Rheinberger original comment on this reads: 'the "scientific real" is a world of traces". Ibid.

From what has been discussed so far, it seems that this study and Rheinberger's share a considerable area of overlap. So, for instance, the third-generation models at the origin of the visual change in cell biology are 'epistemic things', and that they share the same 'space of representation' with microscopical imagery. To reach such a conclusion however, would be to oversimplify the issue. For, to begin with, Rheinberger's study in contrast to this one is not concerned by the possibility of a visible referent, this being a central point at the basis of the difference between the microscopical and the molecular imageries. This last issue will become clearer after our forthcoming discussion on alternatives ways of reading the visual change, (see following subsection on semiotics). I consider that the following statement deserves some attention; for it contains some clues to the extent this study differs from that of Rheinberger's. Epistemic things, he claims, 'are not signs for given objects, representatives of natural entities. They mean what they mean as far as they can be concatenated in spaces of representation'.[554] Rheinberger's statement contains two quite different ideas that do not necessarily correspond with each other and for which I have a different position. Let us start with the second of Rheinberger's ideas, on concatenation and meaning making, an idea with which I agree. To say that 'epistemic things become meaningful by concatenating among themselves' is in fact a different way of saying that, as he put it elsewhere in his book, symbols only 'take their meaning from their relation to other symbols' and that 'there is no representation without a chain of representation'.[555] The reason I agree with this part of Rheinberger's claim is because it is similar to the body of conclusions reached in this study concerning the self-referential characteristics of molecular images of third-generation models (see Chapter 6). Reflecting now on the first idea of Rheinberger's statement, the reason why I disagree with it is because contrary to him, I consider the 'epistemic things' of molecular culture as, in fact, signs, for objects. More accurately put, they are symbols that stand for objects of an invisible nature (see below subsection *'An alternative way to read the visual change: Reading images as signs'*). Moreover, contrary to Rheinberger, who thinks that two visual regimes as the microscopical and the molecular could exist in a single space of representation, I think that although some

554 Rheinberger, 1997, op. cit., pp. 225.

555 Ibid. pp 105.

overlapping is possible they conform two different spaces. The reasons for this disparity arise because Rheinberger's conclusion on this issue is based on a different epistemic-historical situation to the one that this study analyses. He bases his arguments on the work done by cell biologists and biochemists during the 1940s and 1960s when the electron microscope and ultracentrifuge 'representations' combined in assigning biochemical functions to sub-cellular structures.[556] I agree with Rheinberger that in this case the representations (epistemic things) delivered by both instruments were compatible. Nevertheless, in the case of microscopical and molecular imagery this is not always the case, for in many instances their 'graphematic' displays, as we saw in Chapters 1 and 2, just simply do not overlap at all. What is more, as the analysis of the production of images for MBC shows, images of third-generation models, took in many cases a path of their own.[557] Moreover, contrary to Rheinberger's argument that the meaning of epistemic things is not based on the relation of signs with referents[558] I argue that the microscopical and the molecular imageries, as we will see below bear a different relationship to the referent, the cell.[559]

There are a number of other points in which this study differs from that of Rheinberger. Firstly, contrary to his view, this study maintains that 'epistemic things' are not necessarily material objects.[560] He bases his assertion on the idea that rather than being a linguistic process, 'symbol-making, in the realm of scientific activity' is a material one.[561] Although confusing, this position is understandable. Effectively, as the work of Arabatzis on electrons and others shows the material existence of the

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556 See Chapter 1, subsection 1.1.3: *The role electronic imagery in finding functions for structures: From cytology to cell biology (1940s-1960s)*.

557 By this I mean two things on the one hand that in many occasions they were validated by biochemical evidence, independently of microscopic observations and on the other that third-generation models have become self-referential (this last point is fully developed in Chapter 7).

558 Rheinberger, 1997, op. cit., pp. 105.

559 Again a point that would became clearer as the chapter progresses.

560 A conclusion that somehow emerges from our previous discussion on Rheinberger's 'two ideas argument'.

561 Rheinberger, op. cit., pp. 408.

unobservable is a highly controversial issue, hence the difficulties of reaching a clear cut position on the issue. The problem is however, how exactly epistemic things become objects remains unanswered in Rheinberger's work. In a recent critique of his position on the issue, David Bloor arrives at a similar conclusion.[562] Bloor argues that epistemic things exist first of all 'by virtue of being known'.[563] This is another way of saying that epistemic things do not have an existence independent from the practices and the discourses that invokes them as real. Alternatively and in line with Bloor's idea, 'epistemic things', such as the images of third-generation models (signal transduction, membrane embedded receptors and others) present in MBC and other sources are in my view symbolic expressions, which are already invoked as real before they are represented.[564] That is not to say that these symbolic expressions are meaningless or that they have no connections with the 'real' world of cells, which they are supposed to be representing. Symbolic expressions as iconic and even indexical for that matter have to somehow correspond (trade successfully) with the behaviour of the material world.

Lastly, the second point in which this study differs from that of Rheinberger concerns his disregard for the social dimension on the production of 'epistemic things'.[565] As shown by the work of Knorr-Cetina and Amman reviewed here alongside that of Latour and Woolgar, and many others the interactions between the social actors and the agreements reached among them are essential for the creation of trustable and valid 'representations'. As we have shown in the preceding chapter on the production of MBC, it was only through a complex process of visual translation, interpretation, and convention, all based on group agreement and network functioning, that a coherent, 'space of representation' for the molecular imagery came into being.

The above discussion has served to underline the limitations of portraying representations as unproblematic and conceptualising the visual change from

562 Bloor, 2005, op. cit.

563 Ibid. pp. 294.

564 Rheinberger also views science as a symbolic system. Rheinberger, 1997, op. cit., pp. 104-5.

565 A point that he make fully explicit in his discussion with Bloor. Rheinberger, 2005, op. cit., pp. 408-9.

microscopical to molecular imagery as a step forward towards an arguably superior way of representing cells. Essential for challenging this view, which is sustained by most cell biologists, is to show that that these two imageries bear a different relationship to the referent they are supposed to represent, the cell. In the following section this claim is substantiated, for it is at the basis of an alternative way to conceptualise the visual change, which in turn constitutes a central proposal put forward in this dissertation.

### 4.3. An alternative way to read the visual change: Reading images as signs.

To a great extent the epistemologies of cells, that is, what is known about them, what they are taken to be, is constructed from their images. To put it in semiotic terminology, images of cells are signs with an embodied epistemic meaning.[566] In fact, a look at cell biology past and present suggests that it is a visual discipline *par-excellence*. Phrased another way, we can say that cell biology as a body of knowledge is about signs and how the embodied epistemology of those signs is made meaningful for different audiences such as students, professionals, and the lay public. It is somehow curious that images of cells, in particular those not created by visual devices *per se* (microscopes), i.e. those of a molecular nature, have received scant attention as objects of visual analysis. Although there are not straightforward reasons for this, it seems likely that especially in an age of molecularised cell biology the images of invisibles are by and large taken for granted.[567] Images of cells, like the discourses that sustain and frame them, are taken to be universalistic, and trans-cultural, a situation that makes them resistant to questioning

566 Of course this is a two-way system. Images are constructed by their corresponding epistemologies.

567 Molecularised cell biology derives its meaning from the concept of molecularisation. By molecularisation I refer to the condition of conceptualising life almost exclusively as a molecular phenomenon. Molecularisation as an outlook includes explanatory attitudes contained in 19th century physiological and organic chemistry, 19th and 20th century versions of biochemistry and more recently molecular biology. The idea of molecularisation I use here is close to that developed in the following works: de Chadarevian, et al. 1998, op. cit. Kay, 1993, op. cit. Molecularisation has had vast consequences for the practice of biology. One of its latest developments is that of molecular biology, which began by the 1910s, and that has grown dramatically from the late 1970s. It entailed a considerable re-organisation of institutions, specially concerning their practices. My main point is that the drawing of invisible entities, like molecules have been taken as an un-problematically phenomenon by the majority of its producers and consumers in cell biology. I am not saying that this has always been the case, for there were and there are cases in the history of biology where the significance given to visual images in the production of knowledge has been somehow disputed (see later Cambrosio, et al. 1993, op. cit. and Julio M Ottino, 2003, 'Is a picture worth 1000 words'. *Nature*. 2003, 421: 474-76).

and analysis. A visual analysis based on semiotics, for its focus on signs and meaning-making remains thus an important tool for the examination of knowledge construction in cell biology. Moreover, by showing that the microscopical and the molecular imagery bear a different relationship to the referent they represent, (the cell) this visual analysis challenges the view that argues for a progressive substitution of visualities.

Semiotics is the body of knowledge that studies signs and the production of meaning through them. Semiotics analyses how meaning is produced, its main claims being that all human experience is mediated by a complex networks of signs. A significant body of contemporary semiotics is based on the ideas of Ferdinand de Saussure (1857-1913), Charles Sander Peirce (1839-1914) and Roland Barthes (1915-1980).[568] Key conceptualisations from these authors are the ones from which this study builds its methodological framework to analyse the visual change that took place in the discipline of cell biology from the early 1980s.

Of particular relevance for the distinction I am making between two types of images in current cell biology is Peirce's classification of signs in three different types: 'icons', 'indexes' and 'symbols', depending on the quality of the relationship between signs and referents.[569] In the analysis that follows I am relating the three images in **Figure 31** with the three types of existing signs (icons, indexes and symbols).[570]

In **Figure 31**, we confront three different kinds of images of biological material **(A, B and C)**. The first, **(A)**, is the image of an organism known as *Amoeba* obtained

568 Ferdinand de Saussure, *Course of general linguistic*, 1916 (1998 reprint), by Open court Publishers USA. Charles S Peirce, *The essential Peirce* vol I (1867-1893) & vol II (1893-1913). The Peirce edition project. (eds.) Bloomington and Indianapolis, Indiana University Press), 1998. Barthes, 1967, op. cit. Roland Barthes, *Camera Lucida*, London, Vintage Books, 2000. (Original in French, Editions du Seuil, Paris, 1980). Roland Barthes, Mythologies, London, Vintage, 1993 (Original in French Editions du Seuil, Paris, 1957.

569 Charles Hartshorne and Paul Weiss (eds.), The collected papers of Charles Sanders Peirce: Vol II, pp. 135, 143, 44, 169-73, Cambridge MA, The Belknap Press of Harvard University Press, 1960. See also, Peirce, vol I (1867-1893) and vol II (1893-1913) op. cit. Hoopes, 1991, op. cit.

570 This is slightly different to Peirce original distinction in three types of signs, for him considered icons of referents that existed or not.

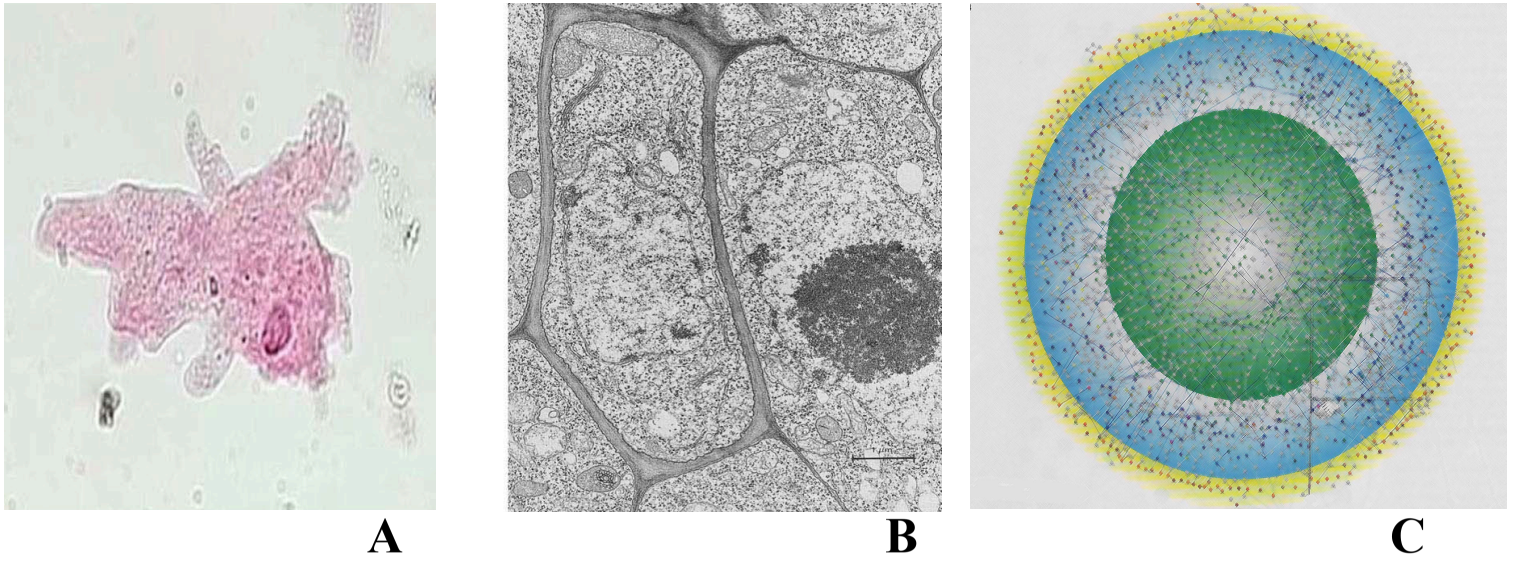


**Figure 31: Images of cells: A)** ***Amoeba*** **as seen through a light microscope x 100. B) Electron Micrograph of a transverse section of a root tip of the bean Phaseolus Vulgaris. Source: de Duve (1984). C) A protein-protein interaction map 'interactome' Giot L,** ***et al.*** **Science (2003)**

with an optical microscope, in its 'natural' living condition (no fixation and staining) and with low magnification (100x). *Amoebas*, are unicellular organisms that measures on average 0.8 x 0.4 mm, that if observed under good light and contrast conditions could be visible to the naked eye. The second **(B)**, is an image of cells from a root tip of a bean plant as rendered by an electron microscope. The third **(C)** is an image of a map of protein interactions in a cell (known as the interactome), produced with the visual output of non-visual instruments (microscopes) through a process of translation (see Chapter 1).[571] Taking into account these images and the different types of signs I conclude the following: The first image corresponds to an icon, that is, a sign whose signifier bears a close resemblance to the object/referent referred to (**Figure 32).** For icons, the sign shows some resemblance with the referent because it possesses most of the referent visual qualities (a resemblance which does not entail a straightforward relationship between them).[572] It is important to realise that in not all observations of cells with an optical microscope a resemblance check between signifier and referent is always possible. In fact the *Amoeba* example is more an exception than a rule. That said, I think it is possible to take an image produced by a lens of low magnification as equivalent to naked-eye observation.[573] The degree of resemblance between the referent (the invisible cell) and its sign for optical and also for electronic microscopy (see above) has an historical background in which new images, taken with increased magnification, are granted a relationship of continuity with previous ones.[574] This relation of visual continuity was first tried by Robert Hooke in his *'Micrographia'*, in 1665. Hooke's achieved this 'iconicity' by showing drawings of ants as viewed with the naked-eye and comparing them to drawings of ants as amplified with a magnifier, so as to establish an implicit relation of visual continuity between both types of images **(Figure 16, A,** see page 77**)**.

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571 This image is known as the 'interactome', a kind of snapshot representing all protein-protein interactions as occurring in cells of the fruit fly *Drosophila melanogaster*. Giot, et al. 2003, op. cit.

572 Joly, 1993, op. cit., pp. 25-32. Of course I accept as valid the point that magnification of a cell by a light microscope is equivalent to getting our sight closer to the object, so that the referent is available for a resemblance assessment. This visual resemblance has a cultural component manifested as a convention to see what you see.

573 The problem that arises here is as van Fraassen points out is until what point this argument for continuity of magnification could be extended. van Fraassen, 1980, op. cit., pp. 110.

574 Hacking, 1985, op. cit.

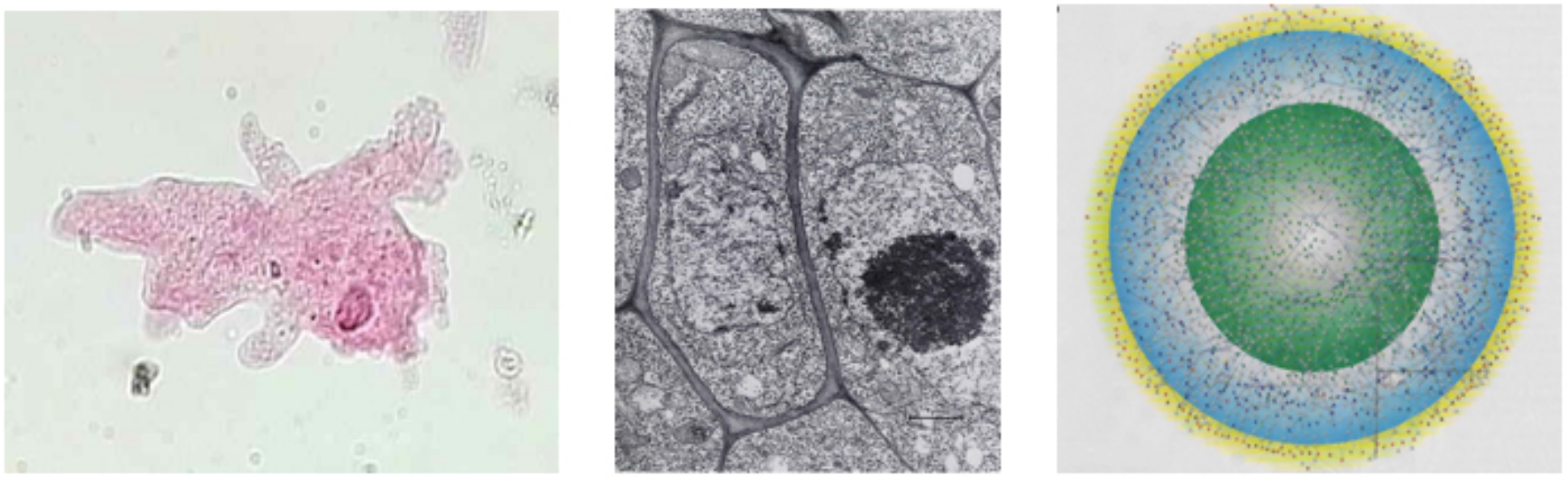


**Figure 32: Images of cells through the semiotic lens**

This ingenious strategy, made his new imagery credible by making them look simultaneously familiar and new.

Turning now to the second image in **(Figure 31, B,** see page 218**),** this could be taken as an index, that is a sign where the relationship between image and referent is perceived as more physically direct or as having a causal relationship **(Figure 32,** see page 220**)**. In this case, this is because of the imprint it has with an optical image (a condition that also endows this image with an iconic character) that is already accepted as valid through the continuity of vision argument.[575] It is my contention that there is a particular instance in the history of modern cell biology where this indexical connection between sign and referent was first made. This was when Porter, Claude and Fullam in 1945 as part of a strategy to refute criticism of the capability of the electron microscope to produce reliable images of cells, created a composite image of the same cell taken with two different instruments to connote similarity.[576] The composed image consisted of two sub-images of the same fibroblasts growing in tissue culture, one alongside the other, one taken with an optical and the other taken with an electronic microscope. **(Figure 33)**. Putting it in semiotic terms they aligned side-by-side two images of the same referent taken with different technologies. Porter et al's, main argument was that in view of the structural similarities between both sets of images the electronic micrographs were up to the job of defining sub-cellular structure (the epistemological claim that mattered at the time). Although this did not fully deflect the criticisms, it was enough to give electron microscopic images the appearance of iconicity - of being 'representing' the real cell, that, that images obtained with the optical instrument have.[577] Porter and his colleague's

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575 The continuity of vision refers to the idea of the existence of a continuum of eye vision that allows us to eventually visually reach the invisible. See Chapter 1, subsection 1.1.2 '*The expansion of microscopical imagery: The electron microscope'*.

576 Keith R Porter, Albert Claude, Ernest F Fullam, Ernest, 'A study of tissue culture cells by electron microscopy: Methods and preliminary observations'. *Journal of Experimental Medicine*, 1945, 81: 233-255, in p.247.

577 What is interesting is that the kind of electron microscopic images that proliferated after that by Porter et al (1945) were those obtained with more drastic chemical treatments, conditions that helped to question the reliability of the instrument to produce valid images.

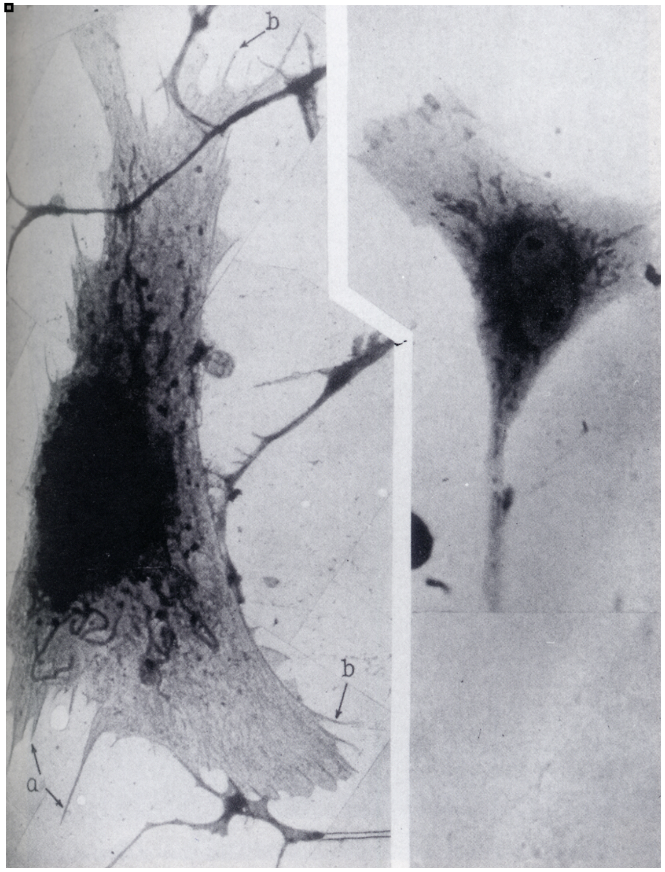


**Figure 33: The construction of indexicality.**
**Electron micrograph (left) and optical image of a cultured fibroblast**
**Porter, Claude and Fullam, 1945**

strategy could be considered as a 20th century update of the one Hooke used in the 17th century to make familiar what was just beyond 'naked eye observations' (see later on the idea of the 'transfer of iconicity').

Another reason why I consider the Porter et al, image to be an index is because the degree of convention between referent and sign at play in it is more significant than for that of an icon (**Figure 32,** see page 220**).** That said it is important to bear in mind that because some causal relations (indexical) appear more obvious to some cultures, epistemic or else than for others, the justificatory steps required to associate the sign to the referent/object could be similar to that of an icon.[578] An important issue worth retaining from all this is that, although this indexicality applies only to this particular combined image (that of Porter et al), it was later associated (bearing the same attributes) by further conventions with the various electronic microscopic images that followed it. In fact this indexicality was the process by which electron microscopic images attained legitimacy to stand for cells from the 1950s onwards.[579]

Finally, the third image in **Figure 31, C**, (see page 218), which presents molecular interactions, taking place inside a cell, images of third-generation models, constitutes a symbol. The status of symbols is based on pure convention (**Figure 32,** see page 220**)**. This is because of the impossibility of direct eye observation of the referent, assuming that the referent exists. In images of third-generation models there is no relation of resemblance between signifier (black dot in a radiographic film) and signified (meaning given to it, proteins interacting). Concerning this last, it is worth noticing that

578 Chandler, view indexes as having a more direct relationship between sign and referent than icons and hence having less elements of convention. Icons and Indexes quite often overlap depending on the image considered. Sometimes the relation between index and icon is blurred because a similar degree of convention is required to understand both. It is even argued that indexes require less convention than icons because of the direct physical connection like the imprint on a bird that walked on the snow (sign), and the bird itself (referent). Some indexical relationships however needs a strong convention, think , for example of the sound of a train for a group of inhabitants of the Amazon whom have never seen a train. Historically indexical signs are viewed as primaries to icons due to photography, the indexical medium *par excellence* (see discussion later). Daniel Chandler, *Semiotics*, London, Routledge, 2002.

579 When talking about conventions it is worth recalling the lengthy discussions that took place to justify the images obtained with the electron microscope On this issue see the following works: Hillman, et al. 1980. op. cit. Rasmussen, 1993, op. cit. Rasmussen, 1997, op. cit.

this could also be argued for the case for the electron microscope image **(Figure 31, B,** see page 218**)** if suspicious about the validity of the continuity of vision argument.[580]

Another key difference among the images **A**, **B**, and **C** from **Figure 31, (**see page 218), is that because of their relation to naked-eye observation each of them derives from different processes of translation. Translation, is 'a process where several steps of 'inscription, transcription, and/or fabrication through a chain of decisions involving several actors, technological devices codes and normative settings will take place'.[581]

Reflecting in our discussion on the main characteristics of the microscopical and the molecular images, it is important to keep in mind the following. Firstly, any visual depiction, involving or not a directly visible to the naked-eye referent will entail a process of translation. Secondly, the nature of the referent, that is the object to be depicted, could range from a tangible/visible object towards a non-tangible one with some other forms in between **(Figure 34)**.[582] A mental concept or a mental image for instance is a non-tangible entity, a conceptual construct used to describe either a visible item like a tree, or a different kind of non-tangible entities, like electrons or different kinds of mental concepts such as 'entropy', 'gravity' or 'alienation'. In the case of, *Amoeba* **(Figure 31, A,** see page 218**)** microscopical techniques and a few words on pictorial conventions would do the trick. In the case of the images obtained with the electron microscope **(Figure 31, B,** see page 218**)** and even more for the case of the images of third-generation models **(Figure 31, C,** see page 218**)** apart from those explanations of pictorial conventions and techniques, a different kind of explanation would be required. One that includes firstly, the complex experimental set up involved in their production, the apparatuses used together with the nature of their output inscriptions; secondly the codes and conventions used to translate the visual output from those instruments (electrophoresis apparatus) into other kinds of visual forms (black stains in autoradiograms), that is the series of interpretative steps to transform those

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580 As many cell biologists were for electron microscopic images during the 1940s and 1950s (see Hillman, et al. 1980, op. cit., and Rasmussen, 1993, 1997 op. cit.

581 Pauwels, 2006, op. cit., pp. 4-5.

582 Adapted from Pauwels, 2006, op. cit., pp. 4.

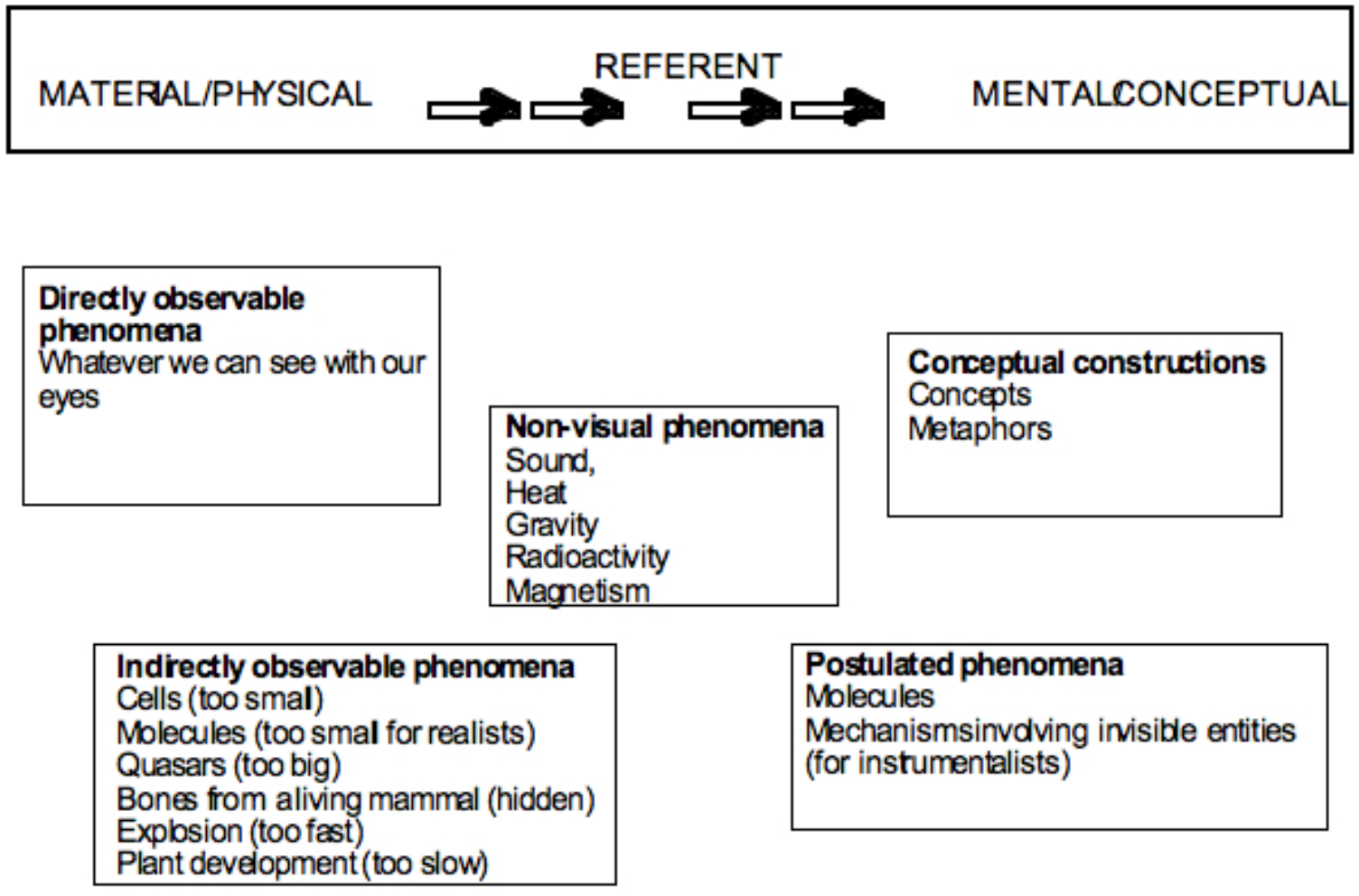


**Figure 34: The distinctive nature of the Referent. Adapted from Pauwels 2006**

inscriptions into images that allegedly account for their existence; and thirdly, the negotiation of what is in and what is out the image among the producers of the images of invisibility. In other words the explanation given of how exactly 'the test tube is filled by traces' to use Knorr-Cetina and Amann terminology.

Back to our main discussion then, despite the fact that behind every image there is a process of translation that transforms the perception of the referent to its final product or image, this process is more straightforward for a directly observable entity than for a non-observable one. It is worthwhile to recall that despite the differences at the level of translation of the three images of cells from **Figure 31, (**see page 218), they all share a common and critical feature. They are all making a historically-dependant epistemic point about what cells are. And that only because of their simultaneous occurrence in current editions of cell biology textbooks do they give the impression that the epistemic point they are rising is the same and that they have the same power to achieve it.

One important consideration is that the process of translation is normally invisible to the audience that is not involved in its production (an issue that as we remarked earlier anthropological and social studies of science had helped to underline). The invisibility of the process of translation when creating images of third-generation models, applies somehow equally to those who produce the images and those who are not involved on their production. In this connection, although, the cultures involved in the production of both types of imagery will be discussed in Chapter 5 it suffices to mention here that other groups not involved directly in the production of molecular imagery, traditional microscopists, have to accept the translational conventions entailed in their production established by others.[583]

The invisibility of the process of translation has two relevant consequences. On the one hand it favours the conceptualisation of the image production process as a 'natural' and/or exclusively based on epistemic reasons rather than as a cultural and historical process. On the second hand, all the processes of translation regardless of the

583 It is becoming more and more difficult to recognise such types of group divisions. In current cell biology practices, practitioners apply different approaches in combination. That said it is still possible to recognise a tradition of microscopists as opposed to molecular biologists.

type of image (visible/invisible) become conflated, resulting in the positioning of the three types of images discussed as belonging to a same culture of image production (when they are not).

An important point to consider is that signs are not mutually exclusive. A sign (an image) can be (can contain elements from) an icon, an index and a symbol, as in the case of composed images like, for instance, Lynch's paired representations for instance.[584] What is more, images in cell biology have grown in complexity, a complexity that entails a combination of elements of iconicity, indexicality and symbolism.[585] Peirce already remarked that 'it would be difficult if not impossible to instance an absolutely pure index, or to find any sign absolutely devoid of the indexical quality'[586]. Chandler gives a good example of this, when he states: 'A map is indexical in pointing to the locations of signs, iconic in its representation, of the directional relations and distances between landmarks and symbolic in using conventional symbols the significance of which must be learn'.[587] When signs combine in a given image however, one of them becomes more 'visible' and hence dominant over the others. This 'preferred viewing'[588] that selects an image as being more, say, iconic than indexical always hinges on a balanced mixture of the following factors: a) how direct is the casual relationship between sign and referent, b) the context

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584 A paired representation refers to a drawing placed alongside an electron micrograph with the aim of facilitating the process of interpretation of the raw image. See chapter 1 subsection 1.1.2 '*The expansion of microscopical imagery: The electron microscope*', for more details.

585 Of course the quality and extent of the conceptualisation of symbols as icons is dependant on the media where it is exhibited. These may vary according to: a) where the image is displayed, i.e. in a textbook or on a scientific article. b) where in the textbook or the article the image is presented, that is on the cover or as part of a textual pattern inside. Either way my argument is that cell biologists preferred reading is that of 'seeing' images of the molecular culture as iconic, as if they were based on resemblance, an outlook that as we saw, ends by concealing its symbolic nature.

586 Chandler D, 'Semiotic for Beginners' at: www.aber.ac.uk/media/Documents/S4B/sem02.html (consulted February 2009).

587 Ibid.

588 Preferred viewing derives from the expression originally proposed by Stuart Hall 'preferred reading' to define one of the alternative ways of reading cultural productions. Stuart Hall, 'Encoding/decoding'. In centre for contemporary culture studies (Ed.): *Culture media language*, London, Hutchinson, 1980.

in which the image is displayed, c) the cultural capital of the viewer[589] and finally' d) the agreement reached by the community of viewers on what exactly to view.

This community-based agreement on what to see has far more important consequences than the selection of a type of sign from a composed image. It is at the basis in fact of how images are selected to construct a given epistemology; a point that takes us into a central issue that this chapter deals with, that of how images of a molecular nature acquire legitimacy and hence power to define what counts as 'real' in cell biology.

### 4.3.1. How images acquire legitimacy to define the real.

We have seen from our previous discussion at least three historically based mechanisms/instances by which microscopical imagery attained legitimacy to stand as 'correct' representations of cells. These were, firstly the comparison of optical microscopic images with naked eye observations (Hooke's case), secondly, the almost physical association between an optical and an electronic image of the same cells (Porter et al, case) and thirdly, the use of a model paired to an electron microscope image adding a theoretical input to it (Lynch's 'paired representations'). I would like to argue in what follows for complementary ways by which molecular imagery achieves this legitimacy.[590]

The legitimacy, of some images and signs to 'represent' an object apart from the internal consistency with the regnant epistemology, the experimental set-up from which it arises and with other images describing related epistemic events, is achieved through

589 Cultural capital is a concept proposed by the French sociologist Pierre Bordieu (1930-2002), originally to explain the educational success of certain groups in 1960s-1970s France. It refers to the accumulated knowledge of and experience over the cultural resources of the milieu by individuals that serves them to gain access to the opportunities that may arise in their environment. This situation put them in advantage over others that don't belong or don't have those cultural resources and/or master the cultural traits of to that social milieu. Although strongly conditioned by class, and the control over economic resources cultural capital is not fully dependant on them.

590 Some of the mechanisms described in what follows such as 'preferred viewing' are not exclusive to molecular imagery since it also applies to microscopical imagery.

three different and related processes. Firstly, as anticipated earlier, by the establishment of a preferred viewing, that is through the decision taken by a given group on what counts as a 'good image', secondly by a process of transfer of indexicality and iconicity on images of a symbolic nature and thirdly, by the linking of these images with a web of meanings from the culture in which those images arise.

### 4.3.2. Preferred viewing.

A preferred viewing is similar to what Ludwik Fleck dubbed as the 'thought style' of a 'thought collective' of scientists.[591] Fleck argued that scientific facts, what is taken as good ('factual') images in our case, are constructed by a distinctive community of interactive scientists' 'thought collectives' that adopt (share) a particular 'thought style', which are defined ways of thinking about a problem shared by that group and learnt during the process of training and specialisation. Although originally designed to account for the acceptability of determined scientific ideas, after reflecting on the production of MBC, it is easy to see Fleck's two concepts fully applying to the case of images. One of the issues I am arguing in this study is that, the preferred viewing taken by the 'thought collective' of molecularisation is to take images of cells belonging to the third-generation models **(Figure 31, C,** see page 218**)** as if they were icons. That is in part because of the role assigned to these kinds of images by their creators, who as a thought collective adhere to the philosophy of ontological realism, the position also adopted by those who consume that kind of images. One of the crucial consequences that this preferred viewing has, as anticipated earlier is that the whole process of image production gets naturalised, thus making access difficult to the codes and conventions embedded in the practices used in the creation of those images (see below on the third mechanism by which images became legitimate). For other groups that consume but do not produce these images (new students, and traditional microscopists in the 1970s when this imagery emerged), it all comes down to accepting the preferred view of them as established by the 'molecular' thought collective. As we saw in Chapter 3 for the case of imagery displayed in MBC, this was achieved by a highly networked process involving many actors, such as students

591 Ludwik Fleck, *Genesis and development of a scientific fact,* Chicago and London, The University of Chicago Press, 1979 (original from 1935). pp 39.

and colleagues, as possible to warrant their participation and hence their endorsement to accept the imagery proposed. The final result then is that highly manufactured images, symbolic images, (third-generation models of molecular imagery) pass for icons, as if molecular lenses existed and hence it were possible to get the same level of 'vision' than as attained by an optical microscope. However, as we learnt from semiotics, with images of a molecular nature it is impossible visually to compare the referent with the image (this is what makes them symbolic).

### 4.3.3. Transfer of indexicality and iconicity into the images of a symbolic nature.

The second mechanism by which images of a molecular nature acquire legitimacy and hence power to define what counts as real in cell biology is through a transfer of indexicality and iconicity from previous images into their own symbolic imagery.[592]
The basic idea behind this should be familiar. When introducing the three different types of signs; icons, indexes and symbols, I accounted, using the case of Porter and his colleagues combined image of fibroblasts **(Figure 33,** see page 222**)** for a specific and historical case of construction of indexicality through iconicity in cell biology. Now I argue for an extension of the process of construction of indexicality through iconicity in cell biology. Because this is a process that makes these images even more resistant to analysis I will discuss some further essential aspects of this process of 'naturalisation' (reification) of the images of molecular visuality in cell biology.

The particular relationship between an object and its representation is what semiotics describes as a dynamic, dialectic and somehow a paradoxical condition between sign and referent. The paradox is due to the coexistence of presence and absence and/or manifestation and latency of the referents in signs.[593] As the two sides of the same coin, an image of a visible (image of the *Amoeba*) although it resembles its object, it is not the object itself (absence). Simultaneously however, the object of the image is present somehow in the image (presence). This ambivalence (absence/presence) of the image has

592 This proposal of images of symbolic nature building their authenticity to define cell events through the sequential transfer of iconicity and indexicality constitutes one of the novelties of this dissertation.

593 Joly, 2004, op. cit.

enormous consequences for things as varied as how signs are interpreted in different cultures and at different times in a same culture. This ambivalence is also important for the connotation images are given in different areas of our culture such as advertising, but also in science and medicine; hence the power images exert on their viewers. (This is a third mechanism by which molecular imagery, I argue, becomes epistemologically authoritative, see discussion below).

The power and relevance of images in other as well as in our former and current cultures is beyond question. A particular example of the importance and power of images is expressed by the famous dictum 'seeing is believing' and the other when we use the expression 'I see' to mean 'I understand'. [594] At the common sense level, for instance, we all know we posit a strong confidence on the ontology (existence) of an object and/or event that we can see with our own eyes when compared to something we cannot see.[595]

The relation between seeing and believing in our present time and culture is taken as being fundamentally different according to whether the visual image is 'made' (drawing, depictions, paintings) or is 'registered' (based on the 'real', photography, television).[596] All registered images (television, cinema) and some 'made' images are of an iconic nature because of the possibility to compare their degree of resemblance to the object/model from which the images derive. It is only for 'registered' images, however, that both categories the referent and its representation can collapse with one another, this being the main reason why there is some conflation between the images themselves and what they represent. This last example, for instance is the situation that is exploited in advertising for instance.[597] Photographic images, 'registered images', contain 'traces' of

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594 As Fox Keller points out seeing also denotes understanding (When we say I see… means I understand). Evelyn Fox Keller, 'Rendre perceptible l'imperceptible', in Jean Pierre Gex (ed.), *Voir l'invisible*, Sophia-Antipolis, France Omniscience, 2007, pp. 15.

595 This is different to the philosophical position of scientific realism, for which, if you can spray electrons that means that they exist. Hacking, 1983, op. cit. The philosophical position of Agnostic instrumentalism, instead only grants existence to what can directly be seen and although recognising the importance of the invisible entities for the explanatory success of theories, it grants a suspended existence to them because of their invisibility.

596 Joly, 2004, op. cit., pp. 13.

597 Ibid. pp. 12-13.

reality (indexicality) because of the almost physical connection they have with the referent. This property of photographic images was noted originally by Peirce who pointed out that the very condition in which photographs are produced (taken), is what makes them perceived as almost being physically linked to the referent.[598] Martin Joly gave this relation of photography to our culture the name 'indexical paradigm', to indicate the deep implications it has for the production of knowledge, that is, for what counts as 'real'.[599] Photographic images are the quintessential example of the 'indexical paradigm' because of their capacity to elicit the real (to make things look as if they were real). Photography as Susan Sontag put it 'has the unappealing reputation of being the most realistic, therefore facile of the mimetic arts'.[600] As she remarks:

> Photographs are, of course artefacts, but their appeal is that they also seem, in a world littered with photographic relics, to have the status of found objects- unpremeditated slices of the world. Thus they trade simultaneously on the prestige of art and the magic of the real.[601]

We normally experience this kind of indexical perception with 'registered images' as a strong relation between image (sign) and object framed and further strengthened by the codes of our culture that take them to be as 'essential truth'.[602] In current situations in our own Western culture for instance, the physical link between a photograph and the referent (event) it portrays, holds the clue to why photographs are used as evidence, as proofs of real events. One characteristic of our Western culture is that this attribute of indexical images (its intimate association with 'real events'), a characteristic that gives them the power of authenticity, has moved beyond their boundaries. In other words, the

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598 Joly, 1994, op. cit., pp. 63.

599 Ibid. pp. 58-61. He contends that: 'If reality has opaque aspects, there are some privileged zones of access, the traces of indexes that allow for its unravelling', pp 60 (my translation). The original in French reads: 'si la réalité est opaque, il existe des zones privilégiées (de traces, des indices qui permettent de la déchiffrer).

600 Susan Sontag, *On photography*, London Penguin Books. 1979 (first edition 1971), pp. 51.

601 Ibid. pp. 69.

602 Joly, 2004, op. cit., pp. 13.

aura of authenticity that indexicality elicits is transferred to images that are not in essence photographic, that are rather of an iconic nature. Such is the case, for instance of 'Magnetic Resonance Imaging' (MRI) and other kinds of scientific images (microscopic or telescopic). Images like these are time and again experienced not as representations, but as the referents themselves.[603] What is more, these embodied 'traces' of indexicality, of iconic images, Joly argues, trigger in viewers a compulsive desire to understand 'images as things in themselves rather than to signs that refer to something'.[604] This, he further argues, 'switches on in viewers a mechanism of fetishist imagery' which is characterised by an idolising type of attitude towards those images.

Taking Joly's arguments further, I would like to propose that in cell biology images of a symbolic nature like of those of the third-generation models of molecular culture **(Figure 18, A and B,** see page 84 an 85 respectively**)** also embody traces of indexicality and of iconicity. In fact, their status arises in part as a consequence of their becoming indexical (they are literally taken as photographs) and in part because they are granted the status of 'mimetic-like' inscriptions (icons). In **Figure 22 (**see page 101), the yellow outer colour, the blue mid-colour and the green central colour represent the cell membrane, the cytoplasm and the nucleus, respectively. The iconic character of images of a molecular nature is built in most cases from the combined action from images of an optical nature plus the continuity of nature argument. Recall the case of Porter's et al electronic micrograph of fibroblasts placed alongside an image taken with the optical microscope. These 'traces' of indexicality and iconicity that the images of the molecular culture have, explain in my view why their viewers (creators and consumers) see them as being 'transparent representations', as being creations with an aesthetic and pedagogical value, and simultaneously as having 'objective' and 'real' like qualities. In short, why the images of molecular interactions as occurring inside cells featured in cell biology textbooks are so appealing, so 'natural' for cell biologists and students alike.

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603 Joly, 2004, op. cit., pp. 12-13. MRI and microscopic images are taken by Joly as equivalent.

604 Ibid. pp. 13. My translation. The original in French reads: 'Ce désir de faire de l'image non pas un signe qui renvoie a quelque chose mais la chose même active un imaginaire fétichiste ou idolâtrique, mais également un imaginaire fusionnel' (By 'imaginaire fusionnel' Joly refers to TV and cinema that give the illusion that there is a total fusion between the image and event, and between the spectator and the world, where the indexical image acts as the true world.

This transfer of iconicity into images of a symbolic nature is not at all exclusive to images of molecular culture. It has been at play in the creation and consumption of other kinds of images from our culture whereas as in science meaning is created. Although this will be discussed below, it suffices to say here that images in advertising, which as we know are of a strong symbolic nature, trigger a complex connotative network of constructed meanings by borrowing from photography this capacity of 'reproducing the real' (indexicality). In other words advertising images exploit the indexical paradigm as if it were of its own regardless that those images are of a symbolic nature. The symbolism at work in advertising, as van Fraassen put it for representations of a scientific nature, also trades on likeness, unlikeness, distortion and addition of new elements.[605]

The meanings of images of a molecular nature get constructed by the particular complex network of connotations with other meanings that again the code of the thought collective allows for. During their creation these images are populated by 'traces' of both indexicality and the iconicity from previous images (from microscopic images for the case of images of a molecular nature) that become hidden from view. Moreover, during the process of their stabilisation and appropriation by other users these images are often taken (read) again as indexical or iconic. That is precisely the case of the symbolic images of the molecular culture, such as the many that populate the different editions of MBC**,** which embody the indexicality from registered images. In their condition of photographs and the iconicity from images of cells from microscopical imagery, their existence occurs in a complex process of visual and cultural translation.

A couple of extra mechanisms reinforce, in my view, the deferred indexicality/iconicity harboured in the images' third-generation models in cell biology. One is to be found in the discourse used to talk about those images that make them unquestionable 'epistemic realities', that is as symbolic expressions, which are already invoked as real before they are represented (see previous discussion on Bloor's critique of Rheinberger's view of epistemic things as material objects), and the other in the visual network of relationships that images began to have among each other mainly in textbooks

605 van- Fraassen, 2008, op. cit, pp. 6.

but also in scientific articles and other media. This is what Rheinberger referred to as symbols taking 'their meaning from their relation to other symbols' and that 'there is no representation without a chain of representation',[606] or to what van Fraassen pointed out, as to be embedded in a 'larger structure',[607] a larger structure that implies the discourses and the episteme to which they connect. After all, images, as is customarily argued for ideas in science, 'become substance only if (they) fit into a dynamic accumulating body of knowledge'.[608]

One of the most important consequences of this deferred iconicity/indexicality that the images of the molecular culture imply is that they end by eclipsing the images of the microscopical culture and consequently concealing many of the epistemic statements they make (see discussion in Chapter 7 on the neglect of the cellular model). By eclipsing images of a microscopical nature they become (for the dominant thought collective) by default (arguably) 'better' images to define the 'real'.

A prime distinguishing feature emerging from our previous discussion is the power of the 'indexical paradigm' for eventuation and definition of what counts as 'real'. In the preface of the second edition (1843) of *The Essence of Christianity*, Feuerbach observed about our era, that 'it prefers the image to the thing, the copy to the original, the representation to the reality, appearance to being'.[609] Feuerbach was writing soon after the invention of the camera; as Sontag argues his comments seems 'as a presentiment' of the impact photography would have. Solid as it may seem, and despite its high esteem as exemplar of the real, the very essence of the indexical paradigm as the hallmark of 'representation' has been contested many times throughout history. Right from its emergence photography has its critiques. As Susan Sontag has signalled, photography was seen as 'parricidal with respect to painting, [and] predatory with respect to

606 Rheinberger, 1997, op. cit., pp. 105.

607 van Fraassen, 2008, op. cit., pp. 30.

608 Mahlon B Hoagland, *Toward the habit of truth: A life in science.* New York, W. W Norton, 1990, pp xx.

609 Sontag, 1979, op. cit., pp. 153.

people'.[610] Scientists, however, completely disregarded this criticism and took photography as the perfect medium to avoid the undesired risks of the subjective contamination of events by the observer. Conceivably because the photographic image as Monique Sicard put it 'become a phenomenon without an observer, an experiment without an experimentalist'.[611] Photography was thus almost immediately adopted in scientific enterprises also because of its new capacity at the time of showing some hidden dimensions of 'real' visible events, such as the horse running (serial photographs of an event almost cinematic), first X-rays images of bones or the splash made by a milk drop.[612] Nonetheless, this position adopted by scientists concerning photography suffered a different challenge to the one described by Sontag. Daston and Galison argue that by the turn of the 19th century the image of photography as warrantor of truth in science was brought into question by 'structural objectivity'.[613] Structural objectivity is a term (epistemic virtue) used by Daston and Galison to refer to a reaction against photographic images (mechanical objectivity), by some logicians, physicists and philosophers who adopted an overall negative attitude to the use of images for the production of knowledge in science. Photographic images, after enjoying time as warrantors of objectivity in science and other areas, began to be strongly criticized as harbouring treacherous subjective traits.[614] Nevertheless, despite this criticism photography survived inside science. Most importantly its ethos of a perfect indexical instance was transferred to other instruments, such as the electron microscope and the autoradiogram.

A more recent and different kind of critique that went to the very core of the authenticity of photography as the indexical paradigm *par excellence*, was proposed by

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610 Ibid. pp. 115.

611 Sicard, 1998, op. cit., pp. 113. Original in French: 'L'image est décrite comme une phénomène sans observateur, une expérience sans expérimentateur'.

612 The sort of images that motivated Keith Roberts. See Chapter 3 subsection 'Roberts' positive and negative influences for the making of MBC'.

613 Daston, et al. 2007, op. cit. I will discuss Daston and Galison's book later in this chapter. See the subsection 'Optical and molecular imageries relationship to the historical dimension of objectivity'.

614 Ibid. Chapter 5 'Structural objectivity' pp. 253-307. I will discuss Daston and Galison's book later in this chapter.

Roland Barthes (1915-1980) in the late 1970s. Barthes exposed the 'illusory character' of the vision of perfect mimesis that photography has on the 'real'.[615] Barthes' key concept to highlight the misleading indexical character of photography was that of 'that was' ('ça a été'). By 'that was' Barthes means that without denying the existence of the referents that they represent, photographs are not copies of the real, but rather a released moment of something real from the past, of something that is not anymore.[616] Photographs are hence 'traces', and if they look specific is because of the traces of indexicality they embody.

### 4.3.4. Constructing the meaning of images through linkages with wider cultural developments.

The third mechanism by which images of a molecular nature acquire legitimacy and hence power to define what counts as real in cell biology is by the linking of images with a web of meanings of a wider nature such as those from our culture and society. The work of Roland Barthes is once again a good referent to assess this process. Barthes, took the classical semiotics developed by Saussure and Peirce into the field of cultural production, a field that later became that of visual semiotics.[617] Barthes original intellectual pursuit was to account for the mystification process at play in our culture that transform small day to day acts into acts of an universal nature, hence his interest in wrestling and advertising.[618]

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615 Joly, 1994, op. cit., pp. 61-5. Roland Barthes, *Camera Lucida*, London, Vintage Books, 2000. (Original in French, Editions du Seuil, Paris, 1980). Barthes was the first to demonstrate the symbolic character of photography, which is overridden by its indexicality.

616 My translation. The original reads: 'La photo n'est pas un copie du réel mais une émanation du réel passe' cited in Joly, 1994, op. cit., pp. 63.

617 The analysis that follows here on signs in cell biology and semiotics is a combination of the views of Saussure and and Peirce, together with some elements of those developed by Roland Barthes. de Saussure, 1998, op. cit. Peirce, op. cit., vol I (1867-1893) and vol II (1893-1913). Barthes, 1967, op. cit. See also: Chandler, 2002, op. cit. Humberto Eco, *A Theory of semiotics* (Indiana, Indiana University Press, 1976.

618 Consistent with his Marxist background, he saw them as a petit bourgeois attempts to deflect the interests of the working class. Hall, 1997, op. cit., pp. 13-74, on pp. 36-41.

The process of signification, or semiosis is based on an interrelationship among the three elements (Peirce's triadic system, **Figure 35)**: First, a signifier, that is the form in which a sign appears (image of cell), second a signified, the sense that is made of it as a mental concept or idea (the epistemological content we gave to it), and third, a referent; the object to which the sign refers (the cell).[619] These three elements, (triangle of signification) operate within a code that relates them. A code refers to all the agreed conditions by a thought collective. Arguably, the current code in cell biology is all the knowledge contained in the latest version of cell theory, which comprises the epistemic claims made by both cultures of knowledge the cytological and the molecular.[620]

Beliefs, values systems and codes from the general culture from where scientific knowledge emerges, those by which we conceptualise, explain and make sense of our experiences inside the cultural space we inhabit, are also of extreme importance for the authority granted to images of a molecular nature.

One of the main features of signs is that they have a connotative dimension. They mean (connote) other than just what the signifier/referent relationship suggests (denotation). They carry this extra meaning that depends more than denotation does on the codes and conventions of our culture.[621] Cases that explain this are abundant from advertising. So, a given product from our culture like a perfume for instance (signifier) connotes glamour, elegance, seduction, etc only in our western culture (code). Glamour, elegance and seduction in turn connect with broader themes and meanings (connotations) in our culture creating thus a complex network, from which they would finally gain their cultural value.[622] In our specific case with cells, the current value attached to the therapeutic potential of stem cells and the special cultural weight given to them by cell

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619 I combine here Peirce triadic system with Saussure' terminology to better link with Barthes ideas on cultural semiotics. For Saussure, only two elements a signifier and a signified constitute a sign.

620 Internal experimental and representational coherence and consistency are of relevance for this.

621 Barthes, 1967, op. cit.

622 Anoher example from the advertising industry is that where for instance a photograph (signifier) of a horse (referent) becomes the signifier of another signified like freedom, virility, etc. Example given by Joly, 1994, op. cit., pp. 136.

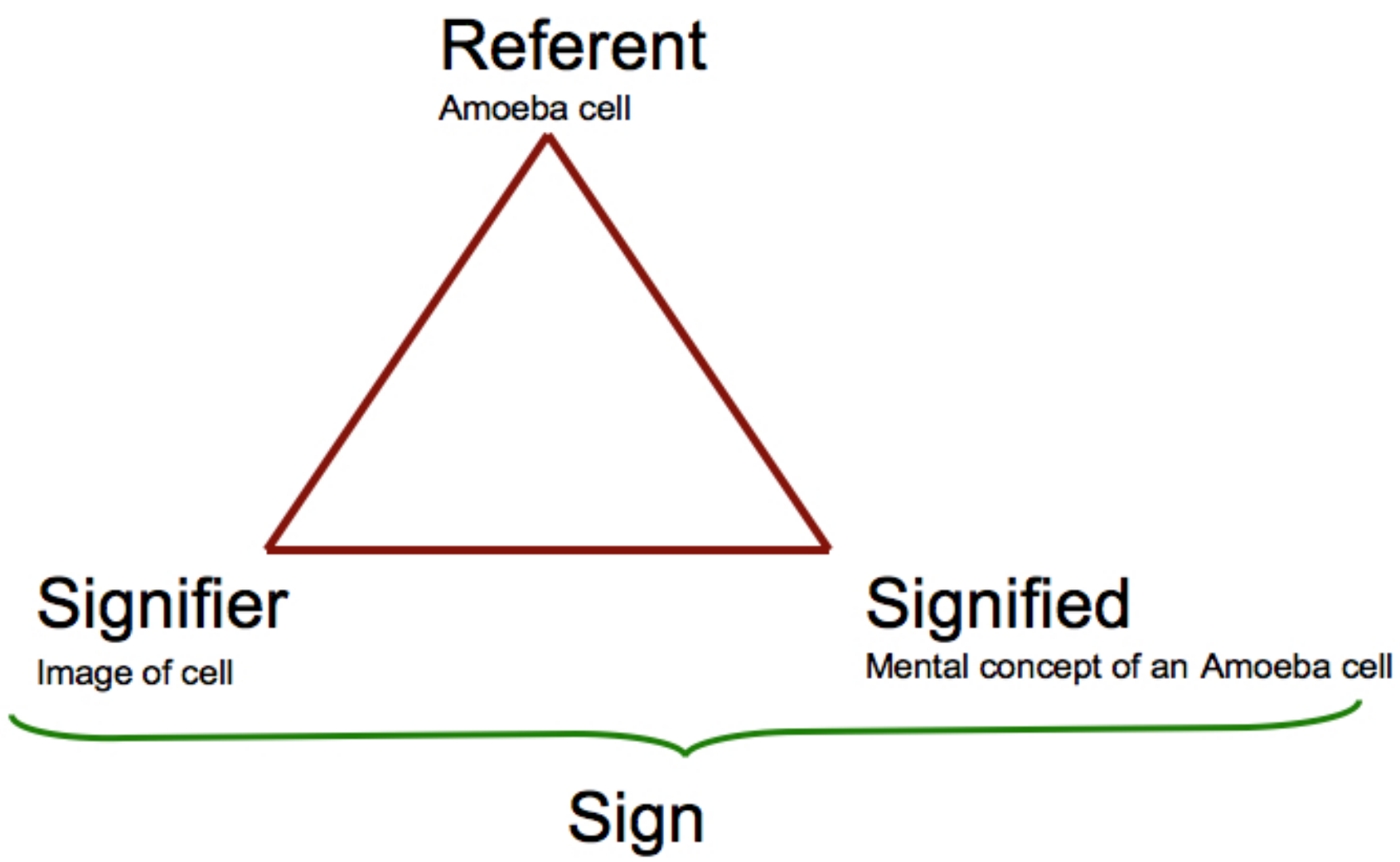


**Figure 35: The triangle of signification**

biologists and the popular views on healing in our times is a good example of the connotative process at work. The process of connotation works by the transformation of a sign from a given triangle of signification into a signifier, which immediately gets associated with another signified to conform a new sign, in a process that might run on *ad infinitum* creating complex networks of signification. Most importantly, as Barthes has suggested, this is the way modern myths are constructed.[623] Myths are commonly viewed by many scientists that disregard the importance of culture and history for the construction of knowledge, as a kind of primitive outlook and hence they are not considered to be part of science. Yet, by reflecting on what science and anthropological studies has taught us about how science construct their meanings and the point Barthes has raised on myths, the former assumption is quickly dispelled. Barthes makes us aware of the ambivalent character of myths and of their social consequences of this ambivalence. Myths are important because regardless of the period in history we look at they help the 'thought collective' that shares them to make sense of their experiences, a practice that sometimes goes beyond the truthfulness that myths may contain. Myths also serve to connect the internal beliefs of a group with the values shared with wider groups. However, myths also transform history into a natural phenomenon placing the knowledge they contain beyond any questioning about its legitimacy and this may have negative consequences. So, for instance the connotation of stem cells as the ultimate solution to all diseases (myth) although important as a claim *per se*, if not cautiously presented to the public, with its for and against points, might give rise to a backlash with negative consequences (specially if the technology shows failure). In this regard a straightforward connection between the use of symbolic (non-resemblance based forms of representation) and normative (ethical) claims on their applicability was made recently.[624]

623 Barthes, 1993, op. cit.

624 Pitt, 2005, op. cit. See discussion of these issues in Chapter 6.

### 4.3.5. Representation and microscopical and molecular imageries the lessons from semiotics.

In the opening paragraphs of this chapter we mentioned that one of the difficulties of the use of the concept of representation resides in its many overlapping meanings with other concepts such as mimesis, resemblance, imitation and copy. This is not surprising since the concept of representation has a long and convoluted historical debate over its meaning.[625] Our current use is in fact based on the inheritance of that condition of indistinct use. So, on many occasions, in papers dealing with issues of representation it is quite common for instance to find the word 'image' denoting 'resemblance' despite that an image, not always entails it.

The current debate over the meaning of representation that goes back in fact to the times of classical Greek philosophy (5th century BC) continues in a slightly different form; that of how independent from mimesis and resemblance representations are. The relevance for this study of the existence of different representations with a different degree of dependence/independence of mimesis therefore resides in the possibility to explore where the microscopical and the molecular imagery locate on that gradient. Phrased as a question, if there is a range of representations from more, to less mimetic, how far away from mimesis the microscopical and the molecular imageries are?

Key contemporary voices in this debate are those of art historian Ernst Gombrich (1960), philosopher Nelson Goodman (1976) and more recently philosopher Bas van Fraassen (2008).[626] At the very heart of their critique of the view of representation as strict mimesis is the idea of the nonsense that it would be for the arts and for science to have representations that merely copy point-by-point the object as it is. As Gombrich

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625 In this regard I found the following source revealing: 'Mimesis' From the Dictionary of the History of Ideas. The University of Virginia Library. USA at: http://etext.virginia.edu/cgi-local/DHI/dhi.cgi?id=dv3-27.

626 Ernest H Gombrich, *Art & illusion: A study in the psychology of pictorial representation*, London Phaidon Press Limited, 2002, first edition 1960. Nelson Goodman, *Languages of Art*, Indianapolis Indiana Hackett Publishing, 1976. van Frassen, 2008, op. cit.

argues, no artist would paint the same picture of the same scene and there is no such thing as a perfect imitation just warranted by the physical reality of the scene the painter is confronting.[627] In a similar line of thought the philosopher Nelson Goodman has labelled as naïve those views that equates representation with resemblance because simply put, any object only resembles itself but not its representation.[628] A representation, he argues, does not copy (imitate) an object, not the way the object is, on the one hand because the object could be a huge myriad of things and on the other because it does not make sense to talk about an exact imitation of an object (illusion of realism).[629] In addition, Goodman believes that resemblance is not necessary for reference, for 'almost anything may stand for almost anything else'. A term like denotation, he thinks, is better to describe what visual 'representation' is.[630] By using this term Goodman opened the doors for representations to trade on codes and conventions, two concepts that as we remarked earlier are essential for the representational success of molecular imagery. The same sort of conclusion about 'representation' and mimesis was arrived at by the philosopher of science, Bas van Fraassen, who argues that it is time, 'to remove the blinders that could focus us naively on the idea that what is represented is simply *like* what is presented in the representation'.[631] Van Fraassen argues that 'representation' not only trades on likeness but also on many other aspects such as unlikeness, distortion and addition (of new elements).[632] Moreover, van Fraassen reminds us of something we have seen at play in the making of MBC. That the way scientific 'representations' make sense and seem so natural is simply because they are made with a purpose in mind. They are

627 Gombrich, op. cit., 2002, pp. 29-44.

628 Goodman, 1976, op. cit., pp. 3-6.

629 Ibid. pp. 6-10. Goodman argues that it is impossible to specify what an object is because for instance, as he put it, 'the object before me is a man, a swarm of atoms, a complex of cells, a fiddler, a friend a fool an much more', pp. 6.

630 He states: 'A picture that represents- like a passage that describes- an object refers to and more particularly denotes it' Goodman, 1976, op. cit., pp. 5. He further claims that: 'Reference to an object is a necessary condition for depiction or description of it, but not degree of resemblance is a necessary or sufficient condition for either' Goodman, 1976, op. cit., pp. 40.

631 van Fraassen, 2008, op. cit., pp. 9.

632 van Fraassen argues that the success of representations such as the caricature of a historical human character for instance depends on a right balance of these elements (likeness, unlikeness, distortion and addition).

basically governed by a set of criteria of adequacy, which pertain to the purpose that the dominant 'thought style' thinks is correct. Building from different examples, like caricature, photocopies of a picture and others, van Fraassen concludes that to understand what a representation means we need to inspect the 'practice of representing'.[633] What van Fraassen is doing is replacing the naïve view on 'representation' (A represents B only if B resembles B) by a more sophisticated one, which has the form (S uses X to represent W for purposes P)[634]. This more sophisticated take on representation is the one adopted in this study, since is a key position for the difference that this study argues does exists between microscopical and molecular imageries.

From this perspective of purpose and practice it is not difficult to see how molecular imagery could be related more than the microscopical one to art. When an artist/scientist confronts a visible object her/his 'representational' choice could go from an imitative, resemblance based one, to an abstract or a symbolic one, with plenty of different combinational forms in between these three alternatives. However, if the artist and/or scientist confronts an invisible object because of the impossibility to imitate it since it simply cannot be seen with the naked-eye, (there is no way to check resemblance between sign and referent), the resultant representation would have all the former elements except resemblance. So this means that if we assume that the depiction of invisibles is possible, then those depictions are better taken as acts of disciplined creation and imagination; acts that freely produce an image that did not exist before. For mimesis independent representations then any kind of explanation, how and on what rules and styles they were achieved, although possible, is not absolutely required. For representations of the invisible Gombrich's maxim (originally proposed for visible entities), 'making will become before matching, [and] creation before reference', become even truer.[635] A debatable conclusion that instrumentalists and constructive empiricists as van Fraassen would be more than glad to reach is that mimetic-independent

633 van Fraassen, 2008, op. cit., pp. 23.

634 Ibid. pp. 28. He uses it but acknowledges that I was first proposed by Giere. Ronald N Giere, *Scientific perspectivism*. Chicago, The University of Chicago Press, 2006, pp. 60.

635 Gombrich, 2002, op. cit., pp. 85.

representations should be taken more as proposals of reality rather than reality itself. Concerning this last point an unexpected consequence of talking about an exact imitation of an object when this is invisible is how, as Goodman points out, the illusion of (naïve) realism takes form. It is this 'intrinsic harmony of thought styles' based on realism, that 'generates a firm belief in a reality existing independently of us' and that makes us forget about the fact, as Fleck put it, that 'cognition modifies the knower so as to adapt him harmoniously to his acquired knowledge'.[636]

It is important to recall that the arguments of Gombrich, Goodman and some of van Fraassen's on representation as independent from resemblance were based almost exclusively on the consideration of visible objects. As such their analysis is partial since, to some extent, it ignores issues of how things are for the case of the invisible. And we must note that this indistinct use is not exclusive to art historians and philosophers, but also to what cell biologists implicitly assume when they engage in depictions of invisible entities. In cell biology textbooks for instance we found in many instances molecular images mixed with statements that treat these depictions as if they were referents.[637] Disregarding the fact that they are the result of measurement, and as such they are not what is being measured, but only as van Fraassen put it, 'what it appears in that particular measurement set up', and appearances are of course not what reality is about.[638]

The preceding discussion adds to my previous conclusion on the semiotic analysis of the three images presented in **Figure 31,** (see page 218), in that we cannot conceptualise them as simply 'representations'. When we talk about microscopical imagery and molecular imagery we are talking about two different kinds of representations, with the first closer than the second relating to mimesis and resemblance. Taking this into account it is my contention that it is more appropriate to conceptualise as

636 Fleck, 1935, op. cit., pp. 86-87.

637 Images of intracellular signalling are given 'real status' by not mentioning that they contain hypothetical models see the texts in Fig 15-42 15-50 and 17-27 for example in Alberts, et al. 1994.

638 van Fraassen clearly distinguish between phenomena and appearances. Whilst phenomena are those directly observable (objects, entities), appearances are the consequence of measurements outcomes. As he put it 'Mars is called the Red Planet not because of its color but because of its reddish appearance as seen or photographed from the Earth'. van Fraassen 2008, op. cit., pp. 9.

representations those, such as microscopical images produced with an optical microscope, where to 'represent', entails the possibility of checking a relation of resemblance (mimesis) between the referent and its visual rendering; and as 'presentations', those as the case of molecular imagery, where that checking for resemblance is not possible and where the free creation of forms is without the constrains imposed by mimesis.[639]

Representation has in my view a component of imitation or 'mimesis', which is inevitable, necessary and thus possible for depictions of the visible. However, this mimetic component is not possible for the depiction of the invisible (because of the direct visual inaccessibility to the referent).[640] This condition far from being restrictive, allows the free expression of the designer when creating pictorial forms. The differences between entities that are observable to the naked-eye and those that are not, but become 'observable' only after an image of them is created, manifest, as we saw previously, when the different images of cells are read as signs and when the technologies involved in their making are explored.[641]

The last point worth highlighting on this issue is that an extra reason why, representation, mimesis and copy have been used indistinguishably from each other is to be found in the association that these words have in our culture with the strongly rooted concept of the existence of 'physical like' reflections of an external world on a mirror like surface in our brain**.** In effect, the original meaning of 'image' comes from the Latin '*imago*', portrait, copy, phenomenon involving a comparison, an inverted reproduction of a given object in a mirror-like surface, originally water, taken later to be the retina, and further later associated with an external surface as in the case of photographic emulsion. This deep-rooted conception in Western cultures runs alongside the one, that understands

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639 Images as that produced by an electron microscope are more resilient to this distinction, for the resemblance check is possible only because the referent is transferred to an optical image. Further discussed in the following subsection: *'Optical and molecular imageries relationship to the historical dimension of objectivity'.*

640 Of course 'to go beyond vision' could be considered as a limitation that could be overcome by technology.

641 Created by the interpretation of indirect technical outputs. Pauwels, 2006, op. cit.

'human knowledge as an assemblage of representations in a 'Mirror of nature'.[642] Both conceptions together are at the basis of an assumed 'unmediated' perception of the external world, one in which observer and the object remains separated. Under this viewpoint, representation is quite often equated to image itself, in that representing is taken to be a reflection of the object in our mind (an image), as a mirror does with any other 'visible' object. It is not difficult to see why then any proposed invisible entity despite lacking a referent is treated as being based on a reproduction of an existent referent in a mirror like surface, creating that illusion of reality that Goodman referred to when discussing the limitations of 'realistic' representations in art.[643] The idea of an independent observer reflecting an object, creating precise mimetic representations as 'mirror of nature' is very entrenched in our culture. Despite important changes on the organisation of vision that took place in the 19th century this conception has survived almost intact.[644] One could in principle think that the change described by Crary involving the fusion between world and observer, eye and instrument in the same plane of operation could be sufficient to erase the confidence in a possibility of total mimesis, one in which one material structure, the brain, perfectly reflects another material structure the world as it is. But this was not the case.

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642 Richard Rorty, *Philosophy and the mirror of nature*, Princeton, Oxford, Basil Blackwell Publisher Limited, 1980. Rorty discuss this concept in its relation to the philosophical ideals of the Enlightenment arguing for the image of scientific theory as mirror of nature, in his case against theology ( pp. 333)

643 Goodman, 1976, op. cit., pp. 34. Without denying the existence of a real world outside our consciousness our access to it is language mediated and as such not based on the idea of a physical like reflection that creates immediate thoughts.

644 Jonathan Crary, *Techniques of the observer: On vision and modernity in the nineteenth century*, Cambridge, Massacchusetts, London England, MIT Press, 1992. Crary's describes a complex change from vision based on stable and fix relations where the observer is separated from the observed, 'individuation' (pp. 14 and 39), the image from the object (pp. 37) that is a separation between interior representation and external reality (pp. 71) to a vision based on training (pp. 112) mobility and exchangeability, a vision abstracted from referent (pp. 14) one where the distinction between observer and the external world blurs (pp71). As he put it, 'In a reversal of the classical model of the apparatus as a neutral device of pure transmission, both the viewer's sensory organs and their activity now are inextricably mixed with whatever object they behold'. (pp. 72).

**4.4. Optical and molecular imageries, relationship to the historical dimension of objectivity.**

Although at first impression the concept of 'objectivity' sounds as of no relevance to this study, a look at a very recent work on it by Lorraine Daston and Peter Galison on the subject, shows that this is not at all the case.[645] Daston and Galison's originality resides in that they have historicized objectivity and defined two key factors: 'scientific selves' and 'epistemic virtues' that have been essential for that history.[646] The correspondence between, the qualities of the contemporary forms of scientific selves and epistemic virtues and those playing a role in the visual shift in cell biology is what make their study relevant for mine. Moreover, because of Daston and Galison's differentiation between 'representation' and 'presentation', in their work it is worth assessing if this distinction holds for the two imageries at the basis of the visual change in cell biology. **Figure 36**, will help to understand the discussion that follows on the whole process of the history of objectivity as proposed by Daston and Galison.[647]

To argue their case the authors review a varied panoply of images as produced and presented in atlases, ranging from the pre-and immediate post-Enlightenment natural philosophy period, through the mid 19th century and 20th century science, into 21st century techno-science. It is not difficult to see why, Atlases, as cell biology textbooks do these days, used to set the standards for how natural or medical phenomena were to be conceptualised and especially acted upon.

As anticipated earlier, a central concept for Daston and Galison's historicity of objectivity is that of 'epistemic virtues'. Epistemic virtues refers to what a correct depiction is expected to look like; how knowledge about nature should be attained, at a particular time in history. Although, at the outset of their work the authors identify three

645 Daston, et al. 2007, op. cit.

646 While, the meaning of 'epistemic virtues' is discussed immediately in what follows, the idea of 'scientific selves' discussed in Chapter 5 subsection *'Some reflections on the makers of epistemic cultures in cell biology: The scientific selves of the microscopical and the molecular traditions'*.

647 Figure 8-4 is an expanded version of the schema presented by the authors, Daston, et al. 2007, op. cit., pp. 413. I felt necessary to expand it because 'hybrid practices', is in my view, treated implicitly by the authors as the latest form of epistemic virtues.

**Right Depiction**

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**Representation**

Based on the idea of fidelity to nature

**Presentation**

Based on the idea of mixing
the artifactual and the natural
and the simultaneity of seeing
and making.

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**Truth to Nature** | **Mechanical Objectivity** | **Trained Judgement** | **Hybrid Practices**

Mid 17th cent. ----------

Mid 19th cent.----------

Mid 20th cent. ----------

Late 20th cent.----------

**Figure 36: The historical dimension of 'Objectivity'. Adapted from Daston and Galison 2007**

types: 'Truth to nature', 'Mechanical Objectivity' and 'Trained Judgement', they add another by the end the book, which they do not clearly define as such, but which I dub 'Hybrid Practices'.[648] Each of these 'epistemic virtues' is associated with well-defined and characteristic 'moral virtues' and particular 'scientific selves'[649]. Daston and Galison are quick to point out that when an epistemic virtue comes into being it does not fully erase the former, but rather amalgamates and deflects the meaning of its predecessors.[650] Much in line with the findings of this study with the microscopical and the different generations of molecular imageries **(Figure 18, A and B,** see page 84 and 85 respectively**),** despite this overlapping, a certain periodisation in which the latest epistemic virtue to emerge dominates over the others is recognisable. 'Truth to Nature' runs from the late 17th to the mid 19th century and is characterised by the selection of images representing ideal types, an object found in nature but idealised as a universal form. Here, interpretation and author input are highly valued. To 'Truth to Nature' follows 'Mechanical Objectivity', from the mid 19th century to the present day that brings about forms of automatisms that minimise scientists' intervention, an attitude that, so it is argued, prevents knowledge from being tainted by subjective projections. Thus, whilst during the 17th century the accuracy of scientific images relied on the moral responsibility of the scientist to be 'true to nature', the advent of photography in the later half of the 19th century changed this moral attitude to 'let nature to speak for itself'; an attitude that implied the elimination of the 'mediating presence of the observer' from the act of 'representation'. In other words, laboratory gadgets like photography by apparently eradicating human intervention started to stand for authenticity.[651] From 'mechanical

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648 Daston, et al. 2007, op. cit., 'Truth-to nature' is discussed in chapter II pp. 55-113, 'Mechanical objectivity' in chapter III pp. 115-190, 'Trained judgement' in chapter VI pp. 309-361 and 'Hybrid practices' as 'Representation to Presentation' in chapter VII pp. 363-415.

649 Discussed in Chapter 5.

650 Daston and Galison made of this historical overlapping of epistemic virtues 'the concept grew historically by gradual accretion and extension from practices', the reason why its history results difficult to seize Daston, et al. 2007, op. cit., pp. 52-53.

651 Mechanical objectivity is in my view one of the epistemic virtues that is strongly experienced by newcomers into science in general and cell biology in particular. The biologists' attitude towards laboratory associated machines, as was the case in the late 19th century for the photographic camera has not changed significantly since. Despite the input they put on the construction and functioning the instruments and techniques of molecularisation they still treat them as 'ideal observers' through which 'nature speaks by

objectivity' follows 'trained judgement', running from circa the mid 20th century to the present, an attitude that consents the expression of artistic elements back into science. Trained judgement, the authors argue, draws from the unconscious to select for intuitive criteria for objectivity.[652] The scientific selves of trained judgement possess an expert ability to see the correct representation through the noise created by the apparatuses they use. What is more, with 'trained judgement' a new kind of pedagogy arose, one that would become very successful in forming self-assured 'trained experts' in the recognition of particular patterns in the representation of phenomena (e.g. Magnetic Resonance Imaging). Finally, the more recent epistemic virtue to emerge (late 20th century), that of 'Hybrid Practices', is characterised by a fusion of artefactual and natural elements resulting in practices where seeing and making are deeply intertwined. The archetype of this epistemic virtue, for Daston and Galison is nanotechnology, the science of manipulation of materials at the atomic level.

The scientific self that constructs the imagery that characterises 'hybrid practices', the authors state, combines the practices and values of scientists, engineers, entrepreneurs and artists in a new fashion. A statement that echoes, as we saw in the previous chapter, many of the epistemic virtues possessed by the leading figures of the team that created MBC, virtues that proved essential for the process of the molecularisation of cell biology. With this epistemic virtue, the characteristic tension between 'active intervention and passive registration of nature' in trying to represent it faithfully, an attitude pertaining to previous epistemic virtues, just disappears.[653]

Key for the epistemic culture of 'hybrid practices' is the equation of images to tools, tools that are involved in simulations of 'seeing and making'. Images of the third-generation models of molecular imagery performing in MBC can easily be equated to tools for 'seeing and making'. For they simultaneously 'see' through 'molecular traces'

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itself'. This attitude ignores the fact that on occasion central aspects of the object under observation might be resistant to detection Pauwels, 2006, op. cit., pp. 9.

652 Daston, et al. 2007, op. cit., pp. 370.

653 Daston, et al. 2007, op. cit., pp. 381.

and ‘make’ cellular conditions, as ‘spaces of representation’, regardless of their relation to ‘the real’. If images ‘represent the ‘real’ or if they are simulations does not matter any longer. What matters is that they are open to an unquestionable and supposedly endless manipulation. As Daston and Galison argue, if in ‘mechanical objectivity’, images ‘aimed to show the actual, rather than the ideal’ and in ‘trained judgement’, images were produced ‘to highlight important features […] or to smooth out the artefacts of production’[654], in ‘hybrid practices’ images became objects and subjects; images are taken to be images-as-tools to simultaneously make and change epistemic things. For ‘hybrid practices’, the authors argue, images ‘function less for representation than for presentation’.[655] One important issue to notice here is Daston and Galison’s use of ‘representation’ and ‘presentation’ to denote respectively representations, which are based on resemblance and those that are not. As they put it, ‘the prefix re-is essential: images that strive for representation present again what already is’.[656] Aware of the non-sense of fully mimetic representations they implicitly assume as van Fraassen does (and as I do) that ‘representation is always an exercise in portraiture, albeit not necessarily one in mimesis’.[657]

It is undeniable that Daston and Galison’s ‘representation’ to ‘presentation’ shift bears some relation to the visual change in cell biology beginning in the mid 1980s that I describe in this study. Microscopical images, could be considered to be part, of ‘mechanical objectivity’ and ‘trained judgement’ and as such, be ‘representations’, that is resemblance related representations that assume a clear ‘distinction between nature and image’. For the case of images of a molecular nature, they rather belong to the epistemic virtue of ‘hybrid practices’, they are ‘presentations’, that is non-resemblance based images where the previous distinction made by mechanical objectivity between ‘nature and image’, becomes blurred. Of course, in spite of their differences it appears clear that

654 Ibid. pp. 385.

655 Ibid. pp. 383.

656 Ibid. pp. 382. To differentiate their distinction between representation and presentation they state that: ‘Representative images may purify, perfect, and smooth to get at being, at “what is”. But may not create out of whole cloth, crossing over from nature into art.

657 Ibid. pp. 382.

images displaying molecular interactions play the same role as exemplars for objectivity as did microscopic photography during 'mechanical objectivity'.

Notwithstanding the many similarities between Daston and Galison's work and this one, there is, nonetheless one slim difference. The change from 'mechanical objectivity' to 'hybrid practices', when taken as a change from the use of images depicting visibility towards another depicting invisibility, is, in their opinion a shift that began to occur in the late 20th century (circa early to mid 1990s) with nanotechnology as an embodiment of it. In my view, this shift began to emerge slightly earlier, by the late 1970s and early 1980s. In fact, the shift from indexical/iconic to symbolic imagery in cell biology that I am describing emerged well before the technological development that Daston and Galison see as being at the basis of 'presentation' kind of images, that is the computer. It is only later, from the 1990s, by the time MBC's third edition of 1994 was published, for example, that this computer-made imagery began to have a significant space in textbooks.[658]

It is possible to identify three senses that Daston and Galison assign to 'presentation', the globalising characteristic of the latest stage in the history of objectivity, that of 'hybrid practices'.[659] Firstly, they take 'presentation' to mean a craft that creates things rather than 'copying what already exists' (representation as mimesis).[660] Secondly, 'presentation' refers to images produced to lure and persuade 'scientifically and entrepreneurially', as images of commodities in our Western consumer culture (see Chapter 6 on hyperreality). Thirdly, presentations could easily pass as 'artistic presentations'. This triple sense Daston and Galison gave to 'presentations' pretty much coincides with, the way I conceptualise the latest form of molecular imagery, that is as mimesis independent representations that use forms not seen by the naked-eye before, hence their artistic and symbolic features. When compared to microscopical

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658 As discussed in Chapter 3, the process of image making in Robert's hands has remained essentially hand-made.

659 Daston, et al. 2007, op. cit., pp. 383-384.

660 For that reason they think is unnecessary to use the prefix (re), which gives the idea of copying or repeating something that already exists.

imagery molecular imagery can embody more elements of 'unlikeness' and 'distortion', (in van Fraassen's terms).

A further concept and a key one, linked to the type of images that characterise the epistemic virtue of 'hybrid practices', is that they are haptic images. Haptic vision refers to a kind of vision that gets combined with our other sensory experience, especially touch to achieve depictions. Their images allows for simultaneously 'seeing' and 'touching' what is being observed. Disappointingly, Daston and Galison do not develop this topic further. Besides, the overall picture the authors give is that haptic images are exclusive to the very recent developments of the tunnel electron microscope and nanotechnology.[661] This is not at all the case however for these kind of images have been around for a long time. The art historian Alois Riegl (1858-1905) suggested that they were part of Egyptian art.[662] Later haptic vision was at the basis of artistic (artisan) and scientific modelling in the 17th, 18th and even late 19th centuries as well as in the practice of early electron microscopists.[663]

### 4.5. Is there a context of justification for molecular imagery?

A central concern in science is the capacity of its theories and models to consistently explain the data arising from experimental conditions. This view, explicitly held by philosophers of science and implicitly by most scientists, has it that science possesses strict controls for the selection and/or validity of theories and models proposed. The factor that limits the selection of theories, so the argument runs is a key criterion, which is at the basis of its own methodology, a criterion known as the context of

661 Daston, et al. 2007, op. cit., pp. 384.

662 Riegl argued that there was a significant historical shift in art from forms that allowed physical tactility as manifested in Egyptian art and its single plane depictions, towards an optical art based on abstract space as manifested in Greek and Roman sculpture. Margaret Iversen, *Alois Riegel art history and theory*, Cambridge, Massachusetts, MIT Press, 1993.

663 See the work of Rasmussen (1997) *'Picture control'* op. cit., where, building on Merleau-Ponty's work he discusses the idea of electron microscopy as a practice of viewing that directly involves the viewer's body.

justification.[664] In science any model or theory can be produced and proposed under any kind of socio-cultural and psychological circumstances (context of discovery). Yet, for this model or theory to be valid, to be able to make a point on the production of scientific knowledge, it should be able (among other things), first and foremost, to offer a satisfactory explanation of the phenomenon which it describes, secondly, it should be consistent with the contextual knowledge to which it belongs, and thirdly, it should be able to predict and create new experimental conditions based on what it proposes, especially in the case of an image of a new mechanism for example (context of justification).[665]

Some interesting thoughts arise concerning 'discovery and justification' by reflecting on the production of molecular imagery by Keith Roberts in MBC. The first point to notice is that he created molecular imagery (based on his five rules of depiction) without any explicit strict criteria for its empirical validation. To put it differently, Roberts' images of cellular processes are more about different free-will like perspectives with few if any specifically designed control for veracity.[666] This looks close to the notions of multi-perspectivism of forms that characterises artistic expressions rather than scientific ones. As we know the very essence of art resides in its concomitant freedom to produce any kind of (in Daston and Galison's words) 'presentations', of 'reality'. Different artistic expressions such as naturalism, cubism, expressionism, abstractionism

664 The context of justification together with the context of discovery were first proposed in 1938 by the German philosopher of science and a member of the logical empiricist movement Hans Reinchenbach (1891-1953). These concepts were originally created in an attempt to distinguish all the inductive steps used to logically justify a theory or knowledge (context of justification) from those psychological and/or sociological factors that conduct to the proposal of a theory (context of discovery). Later in history the content of justification became associated with the output of experimental research. The most common claim associated with both contexts is that what only matters for the development of scientific knowledge is the context of justification. See: Paul Hoyningen–Huene, 'Context of Discovery and Context of Justification', *Studies in History and Philosophy of Science*. 1987, 18:501-15.
The view of both contexts as separate was contested by Kuhn, who argued that the psychological factors involved in the context of discovery continue to play a part in the process of justification. One way how this happens is because values are disguised as criteria (rules) of choice. See Thomas Kuhn, *The essential tension: Selected studies in scientific traditions and change*, Chicago, London, University of Chicago Press, 1977.

665 These are some of the conditions also applicable to the process of theory choice. See Kuhn, 1977, op. cit., pp. 320-39.

666 This of course doesn't apply for all of his depictions, some of which are based on the input of the electron microscope.

and so forth, although based on different codes and conventions, are exempt from the three criteria belonging to the context of justification. It seems therefore that the classical 'justification' process is not as such strictly at play for the production of molecular imagery as it is for microscopical imagery.[667] If there are some validation steps for molecular imagery, they are closer to those applied to classic artistic visual expressions, for its overriding concern as we saw in Chapter 3 when we looked at the making of MBC, is to make a visual story.[668] All that said, it is my contention that molecular imagery, in its quest to explain visually a cellular mechanism for which there is no visible referent, follows a sort of context of justification, albeit a more relaxed and diffused one that the one defined for theories and models. Molecular images are 'justified', by the internal consistency with the epistemology from which it originates, by its correspondence with the accepted translational process from the technologies that produces it, the thought collective that accept them, and finally by the creation of new experiments. That said, as we learn from conceptualising them as signs, molecular images also became legitimate tools for knowledge production from their capacity as symbols to contain iconic and indexical forms as well as from their embodiments of values from the culture from which it emerges. As with the images of invisible molecular interactions at play in signal transduction processes described in the production of MBC, this relaxed context of justification was at work also during the process of image making of electrons. As Arabatzis remarked for the case of electrons, there were in fact several experimental and theoretical constraints that any representation had to satisfy.[669] The 'representation' of un-observables as Arabatzis' put it: has to be rich enough to be able to 'embody all the relevant qualitative and quantitative features of the experimental situations that are taken to be the observable manifestations of the entity in question'.[670] Nonetheless, what is

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667 Think of all the verification processes at play in optical and microscopical imagery to produce reliable, non-artifactual images.

668 It is not difficult to see why, at least in principle, artistic images do not need as scientific images do, any kind of validation steps as those contained in the context of justification True, perhaps an artists have to justify their work to art critics on issues of novelty, creation and /or the framing of their work under a given tradition like abstractionism in painting why they stick to its conventions.

669 Arabatzis, 2006, op. cit., pp. 227.

670 Ibid. pp. 173. That is, any new emergent image on an unobservable entity has to agree with other theoretical views made to explain other relevant features from it. Arabatzis gave two examples: Firstly that of the production of spectral lines, (pp 173). And secondly, the Lewis' model of the chemical bond (pp

clear is that for the case of molecular imagery, due to its art like characteristics, this sort of context of justification is not at all so strict as the logical positivistic position would have liked it to be.[671]

Having framed the microscopical and the molecular imageries as distinctive types of signs and discussed their differential conceptual relation to cells it is time to turn our focus on the main characteristics of the scientific selves of both epistemic cultures and some aspects of the conditions for their historically dependent emergence.

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187-188). In the case of conflicting representations of the electron only after the consolidation of quantum mechanics and the idea of spin they began to amalgamate into a coherent picture. Arabatzis, 2006, op. cit., pp. 235.

671 Ibid. pp. 173. This lax content of justification is also viewed by Arabatzis as cemented together with the context of its discovery.

**Chapter 5. Cultures of seeing and cultures of knowing in cell biology: Image making and the cytological and the molecular tradition.**

In Chapter 1 we saw that a key distinction between microscopical and molecular imageries were the technes[672] that produce them. We also saw how important for both technes to became productive sources of images was their association with two key organizing principles; that of the argument for the 'continuity of vision', and that of the metaphor of the 'window into the invisible world'. Technes and organizing principles, however, become effective as engines of image production only when a particular group of scientists harnesses them and sets the codes and standards in which they operate. The way these elements, scientists, technes and organizing principles, get articulated in different periods is what characterizes the different 'epistemic cultures' conforming scientific disciplines.[673] Although discrete and separated cultures of knowledge production are becoming increasingly difficult to recognise in the current practice of cell biology, due to the fact that most scientists use a combination of technes, it is still possible to establish some differences by looking back in time and comparing different periods. The visual change that this dissertation studies is based, in fact, in a change in epistemic cultures.

A hallmark work on cultures of 'seeing and knowing' competing for representational supremacy in science is that of Peter Galison's *Image and Logic* (1997).[674] Galison's work is a detailed and comprehensive description of a process of transformation in physics from the 1930s to the 1970s, a discipline that like cell biology also deals with invisibles and had undergone an epistemic and visual process of transformation. What Galison's book also does is to relate the visions and functioning of

672 As previously explained I use the term techne to refer to the combination of instrument and technique. Whilst the techne for microscopical imagery are the different types of microscopes together with their particular fixation and staining techniques, the techne for molecular imagery includes the combination of cell culture techniques and lysis, protein electrophoresis apparatuses, radiograms, Immunoprecipitation/Western blotting, two hybrid system experiments, and others.

673 Epistemic cultures is an important concept proposed by Knorr-Cetina referring to a set of arrangements and mechanisms from a given field of knowledge which are bounded through affinity, necessity and historical coincidence to make up what we know and how we know. Karin Knorr-Cetina, *Epistemic cultures: How the sciences make knowledge*, Cambridge, Massachusets, London, England, Harvard University Press, 1999.

674 Galison, 1997, op. cit.

different epistemic cultures to a vast panoply of factors, internal (epistemological) and external to the discipline. This is one aspect that this study is also interested in highlighting as of relevance for the visual change in cell biology (see Chapter 6). Among the internal and external factors to the discipline that had played a role in shaping it, are; the need to describe invisible particles in terms of tangible entities, the support given by industry during the 1930s and 1940s to the development of certain technes such as photography, (new emulsions and films) and the pivotal financial support given by governments and other companies following the end of World War II, support that endured well until the end of the 1970s. As a whole, the coalescence of these factors resulted in a gradual but significant transformation in the practice of physics from individual craftsmanship, a practice typical of the late 19th century, towards a complex network of researchers, each possessing different kinds of skills and approaches.

The great bulk of Galison's comprehensive analysis revolves around the emergence and development of particle detectors such as the cloud chamber, the bubble chamber, the spark chamber and electronic counters. The cloud chamber is an instrument that was first developed in 1895 and belongs to the period of craftsmanship in physics.[675] The cloud chamber is one of the most cherished and more iconic instruments for making visible the invisible world of subatomic particles. Throughout the 20th century however, the cloud chamber competed for primacy in obtaining the most accurate 'representations' of the atomic and subatomic world with other instruments (electronic counters, the spark and the wire chamber). All these instruments were created by different epistemic cultures (traditions in Galison's usage) and were based on a distinct quality of input to account for the existence of sub-atomic particles.[676] The cloud chamber together with nuclear emulsion and the bubble chamber belonged to the 'image' tradition in physics.[677] The image tradition was based on the idea of 'representation' as 'mimesis' and posited images as evidence of a new entity or effect. Counterpoised to it stood the 'logic' tradition, which was based on counting devices that treat statistically enormous amounts of data to

675 Galison, 1997, op. cit., pp. 65-135 (cloud chamber), pp. 313-429 (bubble chamber).

676 Ibid. pp. 20.

677 Ibid. pp. 19-31.

argue for the existence of invisible entities at the atomic and subatomic level.[678] These two traditions were, in Galison's view, not only different in the kind of output they produced (visual images, or numbers) but at the level of their practical aims. Whereas the image tradition aimed at a non-interventionist practice by producing a homomorphic representation of nature, the logic tradition aimed at manipulative practices by producing homologous representations of nature.[679] Both traditions competed fiercely for a 'representational' space in particle physics, a competition that lasted quite a long time (1920s to 1980s). One key reason behind the logic tradition confrontation with the image tradition for 'representational' supremacy was the firm commitment of 'logical experimenters' to eliminate the visual from the production of knowledge in science.[680] During these sixty years of confrontation, the image tradition had a key advantage. The virtue of 'seeing' by the extension of our sense of sight embodied in the cloud chamber was a strong case to argue for its claim to be the best instrument for knowing about sub-atomic particles at the time. This was a powerful epistemic argument at the time for a case against atomistic agnosticism (the suspension of belief in the existence of atoms).[681] The visuality of the cloud chamber would finish by displacing the logic tradition with its indirect statistics-based 'inferences' from its privileged position[682].

The 'image' and the 'logic' traditions went through mixed fortunes among physicists regarding the popularity of their instruments and their epistemologies during the 1920s to the 1970s. From the late 1920s to the early 1930s the logical tradition with its electronic counter seemed to dominate the scene; this changed during the 1950s and

678 Ibid. pp. 19-31.

679 Ibid. pp. 19 and pp. 52. By homomorphic representations of nature Galison refers to those aspiring to 'preserve the form of things as they occur in the world'. Homologous representations instead focus more on the preservation of the logical relationship allegedly to exist among events.

680 Ibid. pp. 40. Also discussed by Daston and Galison in *Objectivity*. They label this position as 'structural objectivity' (see Objectivity, Chapter 15, pp. 253-307.

681 This discussion characterised the world of physics for the first 30 years of the 20th century. See: Charlotte Bigg, 'Evident atoms; Visuality in Jean Perrin's Brownian motion research', *Studies in History and Phiosophy of Science,* 2008, 39: 312-22. Richard O Staley, 'Worldviews and physicists experience of disciplinary change on the uses of classic physics', *Studies in History and Phiosophy of Science*. 2008, 39: 298-311.

682 Galison, 1997, op. cit., pp. 67.

1960s when the image tradition became dominant with its remodeled bubble chamber. By the early 1970s the logic tradition returned to dominance with new electronic detectors[683]. Finally, this competition between traditions and their instruments ended in the early 1980s when they came together and co-existed by producing 'electronically generated, computer-synthesised images'.[684]

Another significant work concerning the theme of cultures of 'seeing and knowing' is that of Carla Keirns on Barbara McClintock's first description of the phenomenon of transposition ('jumping genes') in organisms.[685] Despite being first, McClintock's description was overlooked for many years before being appreciated as a novelty. Evelyn Fox-Keller has argued that this was due to the prejudices against women exerted by a dominant male population that reigned in the emergent field of molecular biology during the 1940s and 1960s.[686] Without denying Keller's conclusions, Keirns argues for further reasons for this neglect. She does so by shifting her focus to a confrontation between two 'cultures of seeing' that existed at the time. The developmental patterns of transposition events in maize kernels detected by McClintock were 'seen' according to the epistemic culture in which she trained. This epistemic culture was based on traditional knowledge of maize development, classical genetic analysis and chromosomal mapping, a kind of knowledge that was alien to that of the new ascendant epistemic culture of molecular biology. Thus, McClintock's 'visual productions' were virtually invisible to the new generation of molecular biologists that through the 1950's and 1960's were busy developing their own discourse and visuality

683 Galison, 1997, op. cit., pp. 20-21.

684 Ibid. pp. 21.

685 Carla Keirns, 'Seeing patterns: Models, visual evidence and pictorial communication in the work of Barbara McClintock'. *Journal of the History of Biology*, 1999, 32: 163-196.

686 Evelyn Fox-Keller, *A feeling for the organism: Life and work of Barbara McClintock*, New York, W.H. Freeman & Co Ltd, 1983. Fox-Keller's book offers one of the most comprehensive accounts of the life of Barbara McClintock from a feminist viewpoint. Keller is quite exhaustive and convincing on unmasking the problems that young women faced in building their scientific careers during the emergence and establishment of new working cultures such as that of molecular biology. McClintock's work on transposition developed between 1950s and 1970s remained obscured to mainstream biologists well until the 1980s when the phenomenon was found to occur in bacteria, which, unlike maize, was one of the chosen organisms of molecular biologists.

that later would start to and end by dominating the field.[687] Because of her epistemological allegiance to the cytological and embryological tradition, McClintock, 'drew what she saw'. The founder figures of molecular biology instead, much in line with the chemical and physical traditions to which they belonged, 'drew what they could infer or reconstruct'.[688] Molecular biologists' visuality was based on the traditional 'presentations' of chemistry, biochemistry and genetics, which relied on the use of molecular models to illustrate 'invisible' molecular structure and the use of cartoons to illustrate 'invisible' mechanisms.[689] In addition, McClintock's experimental practices based on classical plant embryology were perceived as old fashioned and outdated, if not as very complex and laborious, by the ascendant molecular biologists, definitely not in line with the new experimental culture that they had began to apply in their endeavours.[690]

Competition between epistemic cultures over 'seeing and knowing' also occurs when two or more of them overlap in their needs to explain a specific topic in a discipline. When the practices of electron microscopy and biochemistry begin to merge in the 1940s,[691] this was far from being a smooth process, for despite the need and commitment expressed by some cytologists and biochemists to get together into a framework of shared interdisciplinary research, this goal was not an easy one to attain. As Kohler put it:

> Biologists and chemists regarded biochemists as narrow minded specialists, who were no proper chemists nor biologists and who were interested only in the petty

687 Keirns, 1999, op. cit., pp. 176.

688 Ibid. pp. 178.

689 Ibid. pp. 179. It is also argued that schematic images and cartoons suited the reductionist culture to which molecular biology hinged on.

690 Ibid. pp. 179. A running against the clock culture, one characterised by a need of faster results, to which faster growing organisms such as bacteria made more sense rather than the maize with its long generation cycle, complex genetic organisation and intricate development patterns. Keirns quotes the case of a biographer of McClintock and a practitioner of molecular biology confessing that 'most of us were ill prepared- and, I think too lazy- to work hard enough to master the data as it poured forth', Keirns, 1999, op. cit., pp. 179.

691 See chapter 1 subsection 1.1.3 *'The role of electronic imagery in finding functions for structures: From cytology to cell biology (1940s-1960s)'*.

details of metabolic pathways. A. V. Hill wrote: "The trouble with so many biochemists or physiological chemists, or whatever one calls them, is that they either know no chemistry or no physiology or no biology".[692]

Jean Brachet (1909-1988) a scientist with training in both cultures admitted that to work on a hybrid field such as biochemical cytology 'was not accepted easily by either biochemists or cytologists'. He bitterly remembers being accused by an anatomy professor in 1960 at a meeting of 'having produced a dreadful bastard'.[693]

The degree of difficulty in working together for the microscopical and the molecular cultures is reinforced by James Watson who in the second edition of MBG (1970), stated concerning the relation between cytologists and biochemists:

> The chemists and the biologists usually moved in different and sometimes hostile worlds, the biologists often denying that the chemist would ever provide the real answers to the important riddles of biology. Always not to far back in some biologists' minds was the feeling, if not the hope, that something more basic than mere complexity and size separated biology from the bleak, inanimate world of a chemical laboratory.[694]

These different ways of conceptualising the world of living entities also reached a philosophical dimension. Florkin in his classical *A History of Biochemistry* (1972) states:

> It was A N. Whitehead, the philosopher, who posed the question to F. G. Hopkins (a biochemist), whether the modern biochemist in analysing an organism into parts, did not depart from reality to such an extent as to reach a point where his studies no longer had a biological meaning.[695]

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692 Robert E Kohler, *From medical chemistry to biochemistry: The making of a biomedical discipline,* Cambridge, Cambridge University Press, 1982, pp. 333.

693 Jean Brachet, *Molecular cytology*, Orlando, Academic Press, 1985, pp. x.

694 Watson, 1965, op. cit., pp. 37-8.

695 Florkin, 1972, op. cit., pp. 8.

This kind of controversy over the role of imagery on knowledge production is not a new phenomenon. During the last decade of the 19th century and first decade of the 20th century, an intense debate on the role of 'graphic representations' in the field of immunology occurred. Paul Ehrlich was a pioneer on the creation of images of antibodies as tools to explain the observable phenomena of serum agglutination occurring in blood. Some contemporaries, however, disagreed. Jules Bordet, a Belgian immunologist, treated Ehrlich's images of antibodies, the alleged structures present in serum, as 'puerile graphical representations' and consequently argued against their use in immunology. Bordet's critique of Ehrlich 'representations' were of a wider nature. In his view, scientists had to be cautious when using images and diagrams, for they were 'illusory explanations' bearing the inherent danger of 'slippage from model to reality' a practice that, if not tamed, could deflect science from its path of accumulation of experimental facts and data analysis. Ehrlich, in opposition to Bordet, was coherent in his 'chemical approach to immunology', that is with an epistemic commitment to explain biological phenomena from a molecular viewpoint.[696] Ehrlich's imagery, characterised by the 'presentation' of invisibles as an act that precedes their otherwise ambiguous existence (entities that are defined by the very act of presenting them), is among the antecedents for the pictorial practices that became well established and consequently taken for granted in cell biology especially from the early 1980s.[697]

It is not an exaggeration to say that this dispute between Ehrlich and Bordet constituted a defining moment for the role of images in biology. The dispute unfolded at a time when the ontological status of antibodies was in doubt. While the material nature

696 Cambrosio, et al. 1993, op. cit., pp. 674.

697 An interesting feature appears when proposing the existence of new invisible referents to explain biological phenomena: a varied number of signifiers are proposed by practitioners to connect then with those referents. In the case of immunology, for instance, to explain the observable phenomenon of neutralisation of bacterial toxins like tetanus toxins the following names were given for one of its components: 'immune body', 'amboceptor', 'intermediate body', sensitising substance', 'copula', 'desmon'. Cambrosio, et al. 1993, op. cit., pp. 667-668. This plurality of terms as Cambrosio, et al spotlighted, is indicative of a proliferation of referents/objects that have to be yet stabilised. Another important point Cambrosio, et al made, is that all those different names were related to specific theories, in other words they were theory laden. Similar events occurred in cytology by the end of the 19th century when names such as 'colloidal matrix', 'micellae', 'pleons', 'idioplasm', all acted as signifieds for invisible referents.

of antibodies was uncertain Ehrlich's imagery 'materialised' these hypothetical structures. Besides, Ehrlich's representations turned them into 'heuristic devices for subsequent experimentations', in a manner, similar to the images of signal transduction at present.[698] Ehrlich's 'representations' of antibodies have all the characteristics of what Daston and Galison labelled as 'tool images', that is, images for simultaneously explaining and making. Contrary to their view then, these kind of images emerged almost a century before the period they suggest (beginning of the 1990s) with the case of nanotechnology images (see Chapter 4). Moreover, this argument for the direct role of images on experimental practice is at the basis of signal transduction experiments in cell biology from the late 1980s. As such, they are also the base for the emergence in cell biology of a culture focusing on the map rather on the territory (see discussion in Chapter 6).

In most situations in science when new technes develop, a new type of imagery follows suit. Trumpler's work sheds some light on the relationship between new and old imageries for the particular case of neurobiology.[699] She focuses on what became a 'new' key neurobiological problem in the early 1980s when new techniques entered the field, namely the representation of molecules responsible for the transmission of electrical impulses at a cellular level. Before that period, in the early 1950s, the phenomenon responsible for the transmission of electrical impulses was taken to be sodium conductance and was represented by a diagrammatic electrical model. Some years after the techne changed the same phenomenon underwent a representational conversion from 'sodium conductance' to a 'protein channel'. Three main arguments on scientific images are at the core of Trumpler's study. The first, much in line with the arguments displayed in this dissertation on the visual change in cell biology, deals with the role of images in organising the way scientists think. The convergence of different kinds of representation, mathematical, molecular, etc into a single mental image, played a key role in

698 Cambrosio, et al. 1993, op. cit., pp. 682-694. This is an idea originally proposed by Gooding for the work of Michael Faraday. See: David Gooding, '"Magnetic curves" and the magnetic field: Experimentation and representation in the history of a theory', in D Gooding, T Pinch, S Schaffer, (eds.) *The uses of experiment: Studies in the natural sciences*. Edited. Cambridge, Cambridge University Press, 1990, pp. 183-224.

699 Trumpler, 1997, op. cit.

neurobiologists' drive to explore new research avenues, and in the acceptance of 'representations' from other neurobiologists. Here, although Trumpler recognises the difficulties for historians to gain access to these 'single mental images', she boldly argues in line with this dissertation that they are recoverable from neurobiology textbooks. Trumpler's second key point, which differs from the one adopted in this study, is the notion that a new representation (based on the emergence of a new techne), has to correlate somehow with the 'old' representation form it substitutes. This, in my view seems to be more an exception than a rule in cell biology. As this dissertation suggests, when the visual change began to unfold in cell biology by the early 1980s, this change began to overwhelmingly entail a change in research subjects (completely redrawing the old ones such as cell division and emergence of new ones such as signal transduction). Finally, Trumpler argues for a central role for images in science, which is not reducible to language.

The production of new 'representations' has a wider scope that the epistemologies in which they develop, by allowing for a new set of scientific interactions arising between new and old communities of scientists in institutions. As a recent work by Leon Jacyna on the establishment of optical microscopy in Edinburgh during the 19th century shows, microscopy allowed those who more quickly adopted it to differentiate themselves from those who had not and hence to gain institutional advantages.[700] The technology and the culture of the microscope served to install a 'microscopic republic', a cultural regime that changed the ways medical skills were transmitted at the medical school.[701] The optical microscope as an emblem of medical modernity institutionally and epistemologically empowered those seeking for novelty, those who were ready to 'train the eye' to see beyond the anatomy of organs over those who held more conservative views.[702] Key for the installation of this new regime of observation was a growth in the number of converts

700 Leon S Jacyna, "A host of experienced microscopists": The establishment of histology in nineteenth-century Edinburgh, *Buletin for the History of Medicine*, 2001, 75: 225-253.

701 Jacyna, 2001, op. cit., pp. 245.

702 Jacyna, 2001, op. cit., pp. 230-31.

convinced that they were pioneer discoverers.[703] When reflecting on how MBC was produced (chapter 3) it seems we are witnessing a 20th century re-edition of Jacyna's 19th century findings on at the time an emergent microscopical culture, but this time in the hands of the molecular culture.

## 5.1. Some reflections on the makers of epistemic cultures in cell biology: The scientific selves of the microscopical and the molecular traditions.

Epistemic and visual changes in a discipline, as we anticipated at the beginning of this chapter, hinge on actors' actions. Actors' actions, in this case the biologists' actions, are grounded in particular types of 'scientific selves'. Scientific selves as Daston and Galison, have pointed out, internalise and enact characteristic 'epistemic virtues' and these associations have a historical and cultural dimension.[704] The imagery shift that occurred in cell biology from the 1980s is not an exception to that. Each period in fact, that dominated by the microscopical culture (1820s-1970s) and the subsequent one dominated by the molecular (1980s-2000s), has as main protagonist a particular type of scientific self. The moral codes of scientific selves enmesh and interact with wider social conditions to produce a defined body of epistemic practices, at a given moment in history. Of course the demarcation between historical scientific selves, as Daston and Galison suggest, is not absolute, the latest forms always contain elements from the former.[705] Nevertheless as I hope to show in what follows, a clear differentiation exists between the scientific self of the microscopical tradition and that of the molecular one.

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703 Ibid. pp. 245.

704 The concept of 'scientific self' is critical for Daston and Galison's history of objectivity (2007). Although defiend earlier it is worthwhile to recall its meaning again. Scientific self refers to an array of ethical, moral codes and attitudes that are internalised and enacted by scientists determining the practice of science at a given period in history. Different times and different epistemic cultures would have different ethical and moral codes for the pursuit of knowledge hence different times and different epistemic cultures would have different types of scientific selves. See later, subsection 4.4 *'Optical and molecular imageries relationship to the historical dimension of objectivity'*. The correspondence between some of the qualities of the contemporary forms of scientific selves and epistemic virtues and those playing a role in the visual shift in cell biology is what makes their study relevant for mine.

705 Daston, et al. 2007, op. cit.

### 5.1.1. On the authors of *Cell Biology*: the microscopical tradition and the scientific selves of science as a vocation.

The three original authors of CB belonged to the microscopical culture of observation. The images of their research derived by and large from the use of the optical and electronic microscopes. The 'epistemic virtues' that they cultivated and practised belong to a sort of hybrid between 'mechanical objectivity' and 'trained judgement'. To 'mechanical objectivity' because the use of their preferred tool the electron microscope was literally equated by them to photography, that is as a medium conceived to eradicate human intervention and subjectivism and hence standing for authenticity. In using the instrument, however, the authors of CB also showed in their practices some aspects of 'trained judgment'. Their work in configuring microscopical imagery involved the possession of an expert ability to see the correct representation through the noise created by the instrument. Electron microscopists, after the standardization of their imagery, finally became 'trained experts' in the recognition of particular meaningful patterns in the representation of phenomena. It is important to bear in mind that despite the fact that the authors of CB and other cytologists of the time differed from early microscopists over the techne they used, they shared nevertheless strong cultural links with them. They believed on 'the continuity of vision argument', the metaphor of the 'window into the invisible world' and above all that 'beyond the evident complexity of living things lay an essential simplicity'.[706]

The epistemic virtues cultivated by the authors of CB, alongside their practices, have been influenced by the socio-political developments in their countries of origin (Argentina and Uruguay, countries of the Southern cone in general) as well as by the intellectual and technological gap that got established between these two countries and the countries where they learned the science of the time (USA and Europe).[707]

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706 Jacyna, 1983, op. cit.

707 Many of the features enacted by the scientific selves of CB described here will also apply to other contemporary members of the microscopical culture because of their conditions as intellectual émigrés into what are taken to be 'citadels of knowledge' (especially the UK and the USA). George Palade, was born in Romania and emigrated to the USA in 1946, for instance.

Eduardo Diego Patricio De Robertis (1913-1988) (De Robertis for short) was an Argentine cytologist who specialised in the study of mechanisms of neurotransmission.[708] He, together with Dr Francisco Saez (1898-1976), an Uruguayan cytogeneticist with expertise in insect karyotyping, and Dr Wiktor W Nowinski (?-1972), a Polish biochemist interested in the metabolic activity of cells, united their efforts to co-author and publish 'General Cytology' in Spanish in 1946 and in English in 1948. De Robertis, soon after obtaining his doctorate in Buenos Aires in 1939, opened in the mid 1940s, two of the main centres of research in South America, one in Buenos Aires and the other one, together with Francisco Saez, in Montevideo. De Robertis made sure that these two centres possessed all the technology required to practise cytology, including of course the electron microscope. From 1938 to 1947 Saez worked as a professor of genetics in the agronomy department of the university of La Plata, the capital town of the Buenos Aires province, where he founded one of the most important laboratories of cytogenetics in Latin America.[709] Nowinski, an émigré to the US from Poland, worked from the 1940s at the anatomy department of the Medical School of the University of Texas, US where he met De Robertis and Saez.

De Robertis's post-doctoral studies at the Chicago and Johns Hopkins Universities between 1940 and 1948 were on neurosecretion, a trendy theme at the time, being investigated almost exclusively with the electron microscope.[710] In 1953, together with Dr Bennett, his mentor in USA, he managed to get the first 'electromicrographs' of the 'synaptic vesicles', a key structure for the release of neurotransmitters that was still at the time a hypothetical structure.[711] In 1957 soon after returning from abroad for good, he

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708 Claudio A Cuello, Amanda Pelegrino de Iraldi, Jorge P Saavedra, 'In Memorian: Eduardo De Robertis 1913-1988, *Journal of Neurochemistry*, 1988, 51: 1964-5.

709 Thomas F Glick, 'Science and society in twentieth century Latin America', in B Lesley (ed), *The Cambridge History of Latin America. Vol VI '1900 to the Present. Part I Economy and Society*. Cambridge Cambridge University Press, 1995. Alejo Mesa, Carlos Fontaneti, 'Kariotypes of nine Brazilian species of Acridis (orthoptera acridoideal). *Revista Brasileira de Genetica*, 1983, VI, 2: 295-305.

710 G. Rodriguez de Lores Arnaiz, 'Editorial of a special issue dedicated to Eduardo De Robertis' *Neurochemical Research*, 1986, 11:927-932.

711 Eduardo P D De Robertis, Stanley H Bennett, 'Some features of the submicroscopic morphology of synapsis in frog and eartworm', *Journal of Biophysical and Biochemical Cytology*, 1955, 1: 47-58. See Also. Eduardo De Robertis Carlos M Franchi, 'The submicroscopic organization of axon material isolated from myelin nerve fibers', *Journal of Experimental Medicine*, 1953, 94:171-207.

was appointed director of the Institute of Histology and Embryology at the Faculty of Medicine in Buenos Aires.[712] He became president of the International Union of Biological Sciences from 1979 to 1982. As one of his former students and then colleague recalled, 'General Cytology', from 1965 re-branded as 'Cell Biology', was an important factor in De Robertis' campaign for 'modernising medical education in South America', a campaign that sought to offer a more flexible style for career choice.[713] De Robertis was a major player together with Porter, Palade and Claude in the development of electronic imagery. They were pioneers in using electronic microscopy and ultracentrifugation in cytology, an initiative that, as we saw in Chapter 1, was to transform the epistemic content of cytology in the 1940s and 1960s. They kept in fact for many years a close and prolific professional contact. De Robertis and his colleagues acknowledged Porter and Palade in the preface of almost all editions of CB for their criticism and contributions to the production of the different editions of the book.

De Robertis, in common with many of that generation of scientists from Latin America during the 1950s and 1970s, nurtured a particular way of practising scientific research, one based on the idea of science as 'a calling', of science as, an almost sacred, endeavour that would take their countries away from the state of underdevelopment they were in. To build this idea of science they all received direct or indirect influence and inspiration from Professor Bernardo Houssay, the first Argentinean Nobel prize laureate in science for his findings on endocrinology. As one of Houssay's disciples candidly declared, 'I never came across any research group that had not a genetic descent from Houssay'.[714] Many scientists contemporary to Houssay and beyond, aware of his work and his moral attitude to science, wanted to emulate him. Typical were the occasions

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712 Guillermo Jaim-Etcheverry, 'Eduardo De Robertis at 70' *Trends in Neurosciences*, 1984, 7: 138-140.

713 Cuello, et al. 1988, op. cit.

714 Marcelino Cereijido, *La nuca de Houssay: La ciencia Argentina entre Billiken y el exilio*, Mexico, Fondo de Cultura Economica, 1990, pp. 119. The Original in Spanish reads: 'Yo desconocía por completo todo grupo de investigación que no descendiera genéticamente de Houssay'.

when his followers' students and colleagues wondered 'what has to be done to be like a Houssay'.[715]

Houssay's influence on young scientists had two components. On the one hand, it was the science that he practised which was no different to the one practised in the more renowned laboratories in Europe and the USA. On the other, it was his extreme determination to keep the science running in extreme unfavourable situations. In 1943, being deprived of the post he held at the faculty of Medicine in Buenos Aires for his remarks on what he perceived as the government's lack of democracy, he founded an institute of research almost single handed, the Instituto de Biologia y Medicina Experimental (IBYME). The IBYME harboured among its members Dr Luis Federico Leloir who 30 years later would become another Nobel prize winner for his work on the metabolism of carbohydrates.[716] Leloir's Nobel laureate speech in 1970 epitomized what many felt about Professor Houssay. On that occasion he affirmed: 'My whole research career has been influenced by one person, Professor Bernardo Houssay, who directed my doctoral thesis and who during all these years generously gave me his invaluable advice and friendship.'[717]

The young and just graduated De Robertis was not an exception in being strongly influenced by Houssay's scientific and moral values. He followed courses given by Houssay at the university of Buenos Aires and soon after his graduation he received Houssay's encouragement for him to go abroad. It all began in 1935, when at only 22 as a fruit of his delicate sense of observation on histological preparations, using the optical microscope, De Robertis, reported (a new observation at the time) that in most amphibians sex chromosomes cannot be distinguished.[718] This, and other qualities did not

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715 Cereijido, 1990, op. cit., pp. 50 The Original in Spanish reads: 'Que había que hacer para llegar a ser un Houssay'.

716 In: http://nobelprize.org/nobel_prizes/medicine/laureates/1947/houssay-bio.html. Consulted in November 2009.

717 Louis Federico Leloir Nobel lecture 11 of December 1970 'Two decades of resecrh on the biosynthesis of saccharides' In: http://nobelprize.org/search/nobel/?q=LELOIR&i=en&x=0&y=0. (Consulted in December 2009).

718 del Cerro, 2009, op. cit.

pass unnoticed to Houssay who immediately recognised De Robertis's potential 'to develop as an outstanding scientist'.[719] What is more, they shared many things outside the laboratory too. Houssay and De Robertis, in common with many intellectuals during the late 1940s and mid 1950s, strongly opposed the government of Juan Peron in Argentina, who was perceived as a fascist figure. In fact, De Robertis' postdoctoral position at MIT in Boston from 1946 had a component of auto-exile, for he resigned to his post at the University of Buenos Aires as a signal of protest against the government.[720] De Robertis and Houssay also acted together in what was a key event for the development of scientific research in Argentina. In 1956 they joined efforts alongside other scientists to create the Consejo Nacional de Investigaciones Cientificas y Tecnicas (CONICET), an organisation independent from the government that would have as a task the organisation and promotion of scientific research in the country, an organisation of which De Robertis later became a director.[721]

The kind of scientific self that Houssay instilled in his successors such as De Robertis and others was characterised by an attitude of self-denial and almost sacred love for scientific knowledge.[722] De Robertis, in common with Houssay and others, prioritised an almost exclusive dedication to scientific research over any other possible activity. An enormous enthusiasm for the profession was in their view a solution to overcome the temporary scientific deficit they perceived their 'underdeveloped' countries suffered.[723] Their actions were based on the supreme dedication to the ethos of the discipline and an

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719 Cuello, et al. 1988, op. cit.

720 del Cerro, et al. 2009, op. cit., pp.147.

721 Cereijido, 1993, op. cit., pp. 133-4.

722 These characteristics of scientific selves were formulated in Stephen Shapin, *The scientific Life: A moral history of a late modern vocation*, (2008). Shapin's describes the existence of two different types of scientific styles in USA existing before and after WWII. Based on Weber's work 'science as vocation', Shapin argues that before WWII in the USA scientists took their professions as a sacred call to knowledge. Soon after the end of WWII this attitude declined and a new type of scientist emerged, one having a special entrepreneurial style and taking science more as a job than a call (see later on James Watson).

723 Cuello, et al. 1988, op. cit.

almost religious respect for hierarchies.[724] Moreover, they were hard workers, rarely opportunistic, all perceiving the practices and above all the values of science as radically different to those of other professions. They practised science as 'a call to knowledge', a science with a sense of deep professionalism and simultaneously with an air of amateurism.[725] Science for them was not just a job, science was instead, using Shapin's argument, a sort of sacred call for truth.[726] De Robertis, Nowinski and Saez, belonged to a generation for which the quest for knowledge was thus to be first and foremost a vocation.[727] Practicing science as a vocation, as a call for truth turned into a necessity in a country such as Argentina with very scarce laboratory resources and always 'under cyclical institutional instability'.[728] The perception by bioscientists of their profession as a titanic crusade to bring the enlightenment learnt at the 'citadels of knowledge' (USA and Europe) to their own underdeveloped countries, a position that gave them a strong sense of identity, would not stop in De Robertis' generation. It would epitomize in fact the action of many scientists from South American countries that followed them throughout the years.[729]

Among other factors that characterised the authors of CB was their use of a cautious style of writing when presenting findings that in their opinion were of a dubious or not yet fully proven nature. This was similar to the style used by Wilson in *The Cell*. To provide an example, in the third edition (1960) they stated: 'Since many of the theories seeking to interpret cytologic phenomena are still under discussion, we have

724 Recall the case of Porter's culture colliding with the new culture of molecular biologists Chapter 3, subsection 3.2.3 *'The causes of the culture clash: The mechanics of the teamwork writing experience'*.

725 Shapin, 2008, op. cit.

726 Ibid.

727 As remarked earlier, this was also the case of Palade who moved from Romania to the USA in 1946.

728 Rodriguez de Lores Arnaiz, 1986, op. cit., pp. 927-932.

729 Author's own experience as a PhD student in Buenos Aires in the 1980s, time when recombinant DNA technology began to be practiced in Argentina. There was a sense at the time that many of the country's problems such as Chagas disease would be defeated first and foremost in the lab.

sought to avoid them as far as possible and to present the reader only with established facts.'[730]

### 5.1.2. James Watson: Building the scientific self of molecularisation: The Harvard years (1956-1976) and beyond.

James Watson's early scientific career is more than informative about the inner workings of the third wave of molecularisation of cell biology (1970-2000).[731] Watson's, 'epistemic virtues', despite sharing many of the social and academic environments as the classical microscopists, were markedly different. Considering the different epistemic virtues proposed by Daston and Galison, I locate Watson's between those of 'trained judgement' and 'hybrid practices'. Trained judgement because in respect of his work on the structure of DNA (second-generation models) he acted as 'trained expert' by creating spatial patterns from patterns of a different nature (Franklin X-rays diffraction image of DNA fibers). To 'hybrid practices', because both, his model-building skills as well as those needed for the other development that he promoted, that of genetic engineering, required a combination of the practices and values of a scientist, an engineer, an entrepreneur and an artist. Moreover, because both tasks, 3D model building and genetic engineering, required equating images to tools for simultaneous 'making and seeing'.[732] Watson's scientific self, is also grounded, as for the authors of CB, in wider societal developments. These developments, however, as anticipated earlier possessed different characteristics.

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730 De Robertis, et al. 1960, op. cit., pp. vi. Compare with the audacious style of MBC Chapter 3.

731 Here is where the connections between my concept of a 'molecularised cell biology' and those of 'molecular vision of life' (Kay, 1993) and 'molecularisation' (de Chadarevian, et al. 1998, op. cit) get closer (see chapter 1 subsection 1.2 '*The molecular imagery and cytology: An historical overview of its visual forms and its relationship with cytology (the three waves of molecularisation)*'.
The recent work by Shapin (2008) complete the picture of molecularisation by adding important insights on the life of scientists in late modernity (1950s 2000s) in the USA. Shapin, 2008, op. cit.

732 See discussion on Daston and Galison's (2007) concept of 'hybrid practices' in Chapter 4, Genetic engineering is an activity where the difference between knowledge for its own sake and its applicability blurs. As such it constitutes one of the best examples of technosciences as described by Latour.

The further molecularisation of cell biology, its third wave, was made possible by the emergence of recombinant DNA technology throughout the 1970s. The development of this techne did not occur in a socio-cultural vacuum. It occurred in a period of regulation change towards more lax laws, which was sustained by the promotion by governments in USA and Europe of scientific research toward industrial application and consequent profit.[733] This development is connected with an economic trend that began to take place between 1945 and the late 1960s, that of a massive USA government support for science as part of the country's post Second World II economic expansion.[734]

It was during this period (1956), when James Watson took a postdoctoral position, with teaching duties, at the Biology Department of Harvard University. Harvard was at that time in the middle of organisational turmoil concerning two key issues, research initiatives and department organisation. Harvard was not an exception to a trend widespread amongst most universities in the USA that valued a high degree of autonomy for people and projects, as was common in industrial set-ups. That was a time (mid to late 1950s) when, as Shapin put it, 'The American research university has become frankly corporate in its institutional structure, its scale, its financial routines and in many of its ways of recognizing merit'.[735] Corporate changes inside the university system in the USA and Europe were part of other type of changes that began to take shape in western societies from the mid 1950s, those of the consumer culture.[736] From that time onwards governments and private companies synergised efforts to create new goods and new markets (see Chapter 6 for the further expansion of this development).

These deep changes taking place in society as a whole and at universities in particular constituted an ideal scenario for James Watson's plans for biology. The associated budget struggles among the different departments associated with this

733 Wright, 1994, op. cit., pp. 19.

734 Ibid. pp. 21-31. Shapin, 2008, op. cit.

735 Shapin, 2008, op. cit., pp. 230-231.

736 Culture based on the consumption of manufactured standardized products in high volumes. The next chapter discusses further developments of this trend. See Chapter 6, subsection 6.1 *'Western societies in the late 1970s: Times of deep changes at the level of economic production'*.

repositioning was a fertile ground for the molecularisation of biology, as the director of the Biochemistry and Biophysics department at Harvard university from 1948, Paul Doty, had recognised. [737] He asserted that, 'a convergence of events in 1954 created a more promising outlook' for this process of transformation to unfold.[738] James Watson's ideas of making molecular biology a totalising approach inside biology, alongside his eccentric, opportunistic, entrepreneurial and innovative style, fitted nicely with the growing presence of biochemistry labs like Doty's own and others inside the Biology Department of Harvard University. As Paul Doty put it:

> Despite little training in chemistry or biochemistry and lackluster research in the two years following the DNA structure, Watson bravely chose to enter the highly competitive and mushrooming arena of protein synthesis and information transfer from DNA.[739]

There was something about Harvard culture that deeply upset Watson right from the moment he got the job there, and this matched the general perception for the need of institutional reform that Doty, the director, was interested to create by forming a critical mass for biochemistry at the university as a whole. Watson deemed that with the exception of a few, members of the faculty team at Harvard, 'had pedestrian outlooks' and consequently was out of touch with the quality of students that populated it.[740] In his view the department ran an 'uninspiring introductory course' full of 'dull facts' for students to memorise.[741] Dullness, pure facts and repetition were words that deeply upset Watson.

This situation set in motion a key aspect of Watson's scientific self, that of having bold and flamboyant ideas to apply as alternatives to those that were considered old,

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737 Doty, 2003, op. cit.

738 Ibid. pp. 203.

739 Ibid. pp. 204.

740 Watson, 2007, op. cit., pp. 118.

741 Ibid. As we saw in Chapter 3 his position on considering facts in themselves as insufficient will be one of the key attitudes for the writing of MBC.

boring and sluggish, one aspect of his personality that would characterise him, and that would play a key role when he began to write MBG and later plan MBC. Beyond lecturing, Watson's real crusade inside Harvard became that of replacing the classical structure of its biology department, its resource system and its by and large 'descriptive' and 'holistic' aims. No doubts, a pivotal motivation was to gain a position of respect among colleagues and newcomers into the field at Harvard, a fact that would in turn give further impetus to the project of molecularisation that Watson supported. Most importantly however, the creation of opportunities for new PhDs students as well as the creation of new epistemic niches for research was, as ever in any expanding science, an important issue; and 'molecularisation' was not an exception here. All these actions were backed up by Watson's 'entrepreneurial' attitude for innovation in biosciences, an attitude that synchronised well with the growth in business and the acquisition of corporative practices in academia in the USA during the 1960s and beyond.[742]

Entrepreneurialism, a characteristic feature of the scientific selves of molecularisation, is not necessarily one exclusively related to an economic goal. It refers instead to an attitude characterised by opportunism and constant creation of conditions for novelty when whatever kind of endeavour is undertaken.[743] This emergent entrepreneurialism (circa 1950s, 1960s) also has as characteristics the practices of team work, risk taking, opportunism, networking and a high flexibility pattern in the interactions undertaken in those networks. All these 'epistemic virtues' would become later deeply rooted in two key institutions of 20th century modernity, industries and universities.[744] Watson showed some of those epistemic virtues when he interacted with colleagues during the period between 1950 and 1953, the period during which he worked on the structure of the DNA. His insistence to Rosalind Franklin's boss Maurice Wilkins to obtain illegally without her permission the key X-ray image that she produced, a

742 Words such as "entrepreneur', 'expansion', 'new niches', 'innovation', 'novelty', 'risk taking', began to cut across the realms of economics and biosciences from the 1960s.

743 Shapin, 2008, op. cit.

744 Ibid. pp. 231.

critical image that would give him and Francis Crick the critical clue on the helical structure of the DNA is well known.[745]

Entrepreneurialism did not act alone. As we have seen in Chapter 3, there were in fact other values that alongside it configured a core set of attitudes of the scientific self that served as a productive springboard for the development of MBC. Among these values were enactments of familiarity, personal virtue, reliability, self-confidence, charisma, and above all trust. Some of these enacted values that originally belonged to the scientific selves of natural philosophy, will also be essential for the emergence and establishment of late modern (between 1960s and 1980s) techno-science.[746]

The deep organisational changes in industry and academia in the US described above were not of course straightforward ones. Scientific selves enacting charismatic, entrepreneurial and opportunistic attitudes were perceived by many as a process acting to 'reduce the scientist to the level of the hireling', that is to be submitted to the high laws of rational organisation 'rather than to the authority of truth' with the inevitable consequence of transforming science from a vocation to a job.[747] Watson was one of the few who managed to silence those sensible voices that were concerned about scientists losing values from the past. Not only did he possess the new virtues of entrepreneurialism and cultivation for innovation and success, but he also managed to preserve that image of the scientist as a 'priest of nature' with its concomitant 'magic' aura (similar to that possessed by Houssay). The conception of 'priests of nature', which locates the 'inquirer' in a privileged position from which to read the book of life, is associated with the idea of science as a calling, as an almost sacred duty to accomplish. Scientific selves as 'priests of nature characterised natural philosophers from the 17th century to the mid 19th century

745 See for example: Anne Sayre, *Rosalind Franklin and DNA*, New York. WW Norton and company, 1975. Brenda Maddox *Rosalind Franklin: The dark lady of DNA*, London. Harper Collins, 2002.
A recent finding of a letter written by Crick to Monod in December 1961 shows Francis Crick recognizing himself the fact that without Franklin picture, there would not have been double helix. Doris T Sallen 'Despite Franklin's work Wilkins earned his Nobel', *Nature*, 2003, 425: 15.

746 Shapin, 2008, op cit., pp. 5.

747 Ibid. pp. 165. Note that De Robertis and his colleagues belonged to that generation of scientists that believed, in what, Shapin's named (based on the work of Max Weber, 'science as vocation') 'science as a calling' instead of 'science as a job'.

and to some extent manifested in scientists from the microscopical tradition in the 20th century. Arguably, this mixture of old and new features of the scientific self was not exclusive to Watson, for many scientists working in industry and academia also nurtured these aspects of their scientific selves and managed to enact simultaneously science as a calling and science as a job.[748]

For some well-known scientists the issue of new scientific selves enacting a set of new moral codes went beyond sensibilities or doubts. They perceived the new aspects of the epistemic culture that began to be commonplace in academic institutions as a serious drawback for the production of knowledge in biosciences. Erwin Chargaff (1905-2002) a biochemist who made important contributions to DNA studies (the Chargaff rules on the composition of bases of DNA), is the best example of those scientists who viewed molecular biology as an embodiment of the new epistemic culture and thus as a menacing event.[749] He disqualified them *tout court*, in fact, by thinking that 'Molecular biology is essentially the practice of biochemistry without a license'.[750] The scientific selves of molecularisation particularly upset Chargaff. When reviewing James Watson's personal account of the discovery of the structure of DNA, Chargaff remarked that Watson and other people around him 'represent a new kind of scientist', one characterised as having outside ambitions and having faults and vices just as ordinary people have.[751] These scientists, Chargaff added, 'were individualistic, entrepreneurial and willing to bend rules and slight colleagues to get ahead'.[752] In his view, this kind of scientist had lost their

748 Shapin, 2008, op cit.

749 Chargaff found empirically that the number of guanine units equal to that of cytosine units as well as that the amount of adenine units equals those of thymine units (bases) in many organisms. This empirical observation was key for Watson and Crick's proposal of the DNA having a double helical structure where the complementary interaction between bases (base pairing) kept them united.

750 Erwin Chargaff, *Essays on Nucleic Acids*, Amsterdam, London, New York, Elsevier Publishing Company Amsterdam, 1963, pp. 176. Review of James Watson, *The double helix: A personal account of the discovery of the structure of DNA*, London Penguin, 2008, (Originally 1968).

751 Erwin Chargaff, 'A quick climb up mount Olympus', *Science*, 1968, 159: 1448-9.

752 Quoted in Jon Agar, 'What happened in the sixties?' *British Society for the History of Science*, 2008, 41: 567-600, pp. 591.

passion and just 'become passionately ambitious' 'DNA tycoons'.[753] Under those circumstances, he added, 'it has become very difficult to distinguish between what is an ardent search for truth and what is a vigorous promotion campaign'.[754] Chargaff's retrospective charges against Watson and the practices of molecular biology may sound extreme, but they held some truth on the transformative aspects that began to unfold in those years and that would end by making cell biology an almost exclusive molecular science.

Watson fully embodied the new type of scientist that was so determinant for the development of new and bold ideas like the molecularisation of biology by molecular biology and the creation of diverse means to achieve it. Watson's view of the modern scientist as a competitive person in a 'fierce race for breakthroughs'[755] was not only irresistible for many, but it was the best example to follow for those who were involved in molecularisation projects. As we have seen before (chapter 3) these attributes of the molecular epistemic culture proved important for the making of MBC. In fact those who during its making practised 'team work' and 'networking' were sustained by Watson's example and attitude.

Watson's scientific self, formed at Harvard served as an exceptional role model for the new scientists/entrepreneurs of the 1970s molecularisation and commercialisation of the biosciences, a process that just commenced in those years and that would reach a climax with the creation of the human genome project.[756] His years at Harvard were very instructive for Watson who not only nurtured his managerial skills, the ones that would play for him a key role when he became the director of CSH Laboratories in 1968, but

753 Chargaff, 1968, op. cit., pp. 1448-1449.

754 Chargaff, 1963, op. cit., pp. 176.

755 Shapin, 2008, op. cit., pp. 218.

756 Watson's entrepreneurialism never adopted the venture capital search for economic opportunities (cash nexus) that began to emerge at the time (1970s) as others did (Craig Venter case). Although he encouraged that sort of outlook, he strongly opposed a full blown commercialisation of biology. Two cases prove this point. Firstly, in 1974 he openly opposed the creation of a company to sell restriction enzymes out of an academia lab (Cold Spring Harbor). McElheny, 2003, op. cit., pp. 189. Secondly, he took an open position against the patenting of the sequences found in the human genome project (Shapin, 2008, op. cit., pp. 225).

also his lecturing skills.[757] Both set of skills, particularly those concerning the ability to convey the ethos of a 'burgeoning molecular revolution' to an increasing number of students and his ability to transform 'newcomers' into committed cavaliers of molecularisation was to be a key factor in the molecularisation of the life sciences to which cell biology was not an exception.[758] One of those students, Bruce Alberts, the first author of MBC and currently editor of the journal *Science*, openly recognised Watson's capacity to convey the ethos of the 'molecular revolution' to students. In a commemorative book dedicated to him, published in 2003, Alberts stated:

> My many interactions with you have taught me something very important about leadership. Successful new initiatives generally originate from the inspiration and energy of one or few individuals' […] 'Because of your two major textbooks (he refers to *Molecular Biology of the Gene* and *Molecular Biology of the Cell*), extending over 40 years, an enormous number of scientists have greatly expanded their view of biology.[759]

In the same commemorative book, Keith Roberts (the person who did the drawings for MBG and later MBC), also recognised Watson's capabilities to push forward the molecular initiative. He remarked:

> Without hindsight, I am absolutely certain I would never have been involved in drawing many thousands of molecules and cells over nearly four decades if Jim had not had faith in me from the beginning. It is also probably true that without the example of Jim's scientific enthusiasms for molecular and cell biology, I would not have made the precise career choice I did.[760]

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757 It is argued that he transformed CSH, considered to be a decaying centre before his arrival, into an 'institution that become dedicated to promote the molecular culture worldwide' by organising courses as well as theoretical and lab practical publications. (See: David L Luke III, Vision, innovation, breadth and strength', in J Inglis, J Sambrook, J Witkowski J (eds), *Inspiring science: Jim Watson and the age of DNA*, Cold Spring Harbor Laboratory, 2003, pp. 345-8. William Grover, 'An architect at the lab: Some personal recollections, in J Inglis, J Sambrook, J Witkowski J (eds), *Inspiring science: Jim Watson and the age of DNA*, Cold Spring Harbor Laboratory, 2003, pp. 357-61.

758 Doty, 2003, op. cit., pp. 205-206.

759 Bruce Alberts 'What I have learned from Jim', in Inglis, J Sambrook Joseph, J A Witkowski (eds), *'Inspiring science: Jim Watson and the age of DNA'* J R (Cold Spring Harbor Laboratory, 2003, pp. 433.

760 Roberts, 2003, op. cit., pp. 440.

Last but not least, the institutional conditions at Harvard were also of extreme importance for the development of Watson's writing skills. While there he wrote MBG, (1965), the first textbook designed to captivate young scholars into molecularisation, a textbook that was in fact the end product result of both years of molecular genetics research and his lectures at Harvard.[761] The entrepreneurial dexterity, the art of community public relations and fundraising that Watson mastered were outstanding. So outstanding in fact that as Abir-Am put it:

> Watson importance derives not so much from his discoveries or scientific ideas (other than the double helix, of course) as from his remarkable ability to recruit and shape the careers of the next generation of scientists and from his various projects for spreading DNA literacy through outreach, education and publishing.[762]

The picture emerging from our previous discussion here and in Chapter 3 is one in which it is possible to recognise an overall change in the scientific practices that made the discipline of cell biology, practices that are enacted by different types of scientific selves. It is thus clear that the scientific selves of molecular culture began to practice a different set of moral codes and attitudes to those practiced by the scientific selves of the microscopical tradition. Two essential differences are to be found on the display by the scientific selves of molecular culture of a networked-based type of entrepreneurialism and flexible practices. Since this phenomenon occurred during a particular period of the economic, political and cultural development of Western societies (mid 1970s to mid 1980s), the next chapter explores how connected were these wider societal changes with the visual change in cell biology.

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761 McElheny, 2003, op. cit., pp. 115.

762 Pinina G Abir-Am, 2004 'Watson's World'.
At: http://www.americanscientist.org/bookshelf/pub/watsons-world (consulted August 2008).

## Chapter 6. The visual change in cell biology its wider socio-cultural connections

In chapter 5 we discussed some developments that were determinant for the academic environment in which James Watson, a key 'scientific self' of molecularisation, began to nurture his professional expertise. We have seen how from the 1950s onwards academia in the USA began to mimic the functioning of industrial settings with the aim of creating new working conditions that ended by facilitating the transformation of science as a 'calling' to science as a 'job'.[763] This transition allowed the development of a distinctive type of 'scientific self', one able to embody a new moral code based in a new form of entrepreneurialism. This emergent form of scientific entrepreneurialism alongside 'networking' would become paramount for the molecularisation program for biology and for a new set of 'big science' projects that began to emerge in the 1980s with the extensive use of DNA recombinant technology, a process that would reach a pinnacle with the development of the human genome project.

### 6.1. Western societies in the late 1970s: Times of deep changes at the level of economic production.

The visual change in the discipline of cell biology coincided in time (1970s-1980s) with the emergence of a new array of wider societal changes in Western developed societies, changes that entailed a gradual replacement of classical forms of industrial production by new ones.[764] Although, this was a complex, multisided and controversial process, its main characteristics could be summarised as follows. Promoted by global economic fluctuations, and with a clearer program from the early 1980s, the interests of industry and governments, chiefly in the UK and the USA became unified. As a way out of market fluctuations massive efforts were put into initiatives oriented to increase profits by reducing the turnover time of capital.[765] Key for this was the creation of novel consumption niches aimed at a more diversified and individualised groups in

763 Shapin, 2008, op. cit.

764 Krishan Kumar, *From post-industrial to post-modern society: New theories of the contemporary world*, Oxford, Malden Massachusetts, 1995.

765 Harvey, 1990, op. cit.

society. One important incentive for the sustainability of this new pattern of consumption was the possibility for companies to relocate their production abroad, assuring tax avoidance and cheap labour, a process that was facilitated by the ease of travel and communication.[766] The new pattern of production/consumption established by the global operations of companies had the guarantee of non-intervention from the neo-liberal states' chiefly, USA and Britain, interested in promoting a free market economy, as opposed to a state-controlled one.

Key for the expansion of the consumption niches was the replacement of the existing pattern of industrial manufacturing, which was based on the production of high volumes of standardised products, known as Fordism, by a more diversified and flexible one.[767] The new way of manufacturing that became established, known as 'flexible specialisation', is characterised by the quick production of small volumes of goods (according to faster market demand) and directed to more fragmented niches of consumption using new technologies and a skilled and highly adaptable workforce.[768] For the new production/consumption regime of flexible specialisation the encouragement of innovation, fast adaptability to new conditions and more interconnected, less hierarchical types of organisation became paramount.

Marketing and advertising were to play a central role in this process of selling of goods and services to an increasing number and more diversified groups of people, but for that it needed to experiment with new forms and strategies.[769] The 1970s were a decade (already gathering momentum from the 1950s) when professions such as

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766 The facility of air travel and the development of computer technology facilitated this phenomenon.

767 John Allen, 'From Fordism to post-Fordism', in S Hall, D Held, and T McGrew (eds), *Modernity and its features,* Cambridge, Oxford, Polity Press and Blackwell Publishers Ltd, 1992, pp.170-204.

768 Peter Braham, 'The divisions of labour and occupational change', in J Allen, P Braham and P Lewis (eds), *Political and economic forms of modernity*, Cambridge, Oxford, Polity Press and Blackwell Publishers Ltd, 1992, pp. 275-314, on pp. 302-9. Allen, 1992, op. cit. John Allen, 'Fordism and modern industry', in J Allen, J Allen and P Lewis (eds), *Political and economic forms of modernity,* Cambridge, Oxford, Polity Press and Blackwell Publishers Ltd, 1992, pp.230-260.

769 A massive expansion of new audiences was met, targeted by, an increase in more sophisticated forms of advertising Daniel Bell, *The cultural contradictions of capitalism*, New York, Basic Books 1996 (original 1976), pp. 68-9.

marketing and advertising were to some extent 're-invented', expanded, and put to work on a massive scale in new areas.[770] One of the most remarkable consequences of this economic and cultural process as a whole was the fact that images and appearances began to have the same weight as the materials things to which they referred.

As suggested earlier, a central element for this transformation in production and consumption patterns was the emphasis and prominence given, at different levels, to interactivity and networking for functioning among groups inside and outside companies.[771] This become so central that as Manuel Castells put it, 'networks constitutes the new social morphology of our societies, and the diffusion of networking logic substantially modifies the operation and outcomes in processes of production, experience, power and culture'.[772] Network culture became a central organising principle for the enactment of practices by social actors in most social scenarios, including the scientific. In the case of cell biology, which at the time (early 1980s) was undergoing a new 'wave' of molecularisation networking, it is my contention that networking became a new organising principle. In fact my analysis of the production of MBC allows me to argue that networking articulated in productive ways with the key organising principles of the 'window into the invisible world' and 'the continuity of vision argument' to sustain the development of the latest forms of molecular imagery in cell biology. Put simply, networking was a key component of the visual change. One interesting aspect we learnt from the production of MBC (Chapter 3) is that a high output networking functioning

770 See Chapter 3 subsection 3.2.1 and 3.2.2 on the role of Gavin Borden and Miranda Robertson on the production of MBC. Advertising expenditure grew enormously from the 1960s and kept growing during the 1970s as part of corporate strategies to sell their products and create a positive image. Harvey, 1990, op. cit., pp. 160.

771 Networks as systems of communication and information exchange have been a key component for the functioning of several enterprises ranging from economics groups to natural philosophy and later institutional science. In biology for example, the conditions, in which molecular biologists worked on the 1960s suggests that some sort of networking was in place. Francois Jacob, *The statue within: An autobiography*, Basic books, 1988, pp. 286. The kind of network I refer to here however uses new technologies and more complex and interrelated ways of functioning, such as multiple relationships with other networks and so forth (see chapter 3).

772 Manuel Castells, *The rise of the network society*, Massachusetts, Oxford, Blackwell Publishers Ltd, 1996, pp. 469. As Kress an van Leeuwen put it 'The network is modelled on a form of social organisation […] in which it is difficult to, if not impossible to form a coherent view of the whole. Perhaps it is not accidental that this kind of network is coming to the fore in an age of increasing social fragmentation and regionalisation'. Gunther Kress and Theo van Leeuwen, *Reading images, The grammar of visual design*, London, Routledge, 1996, pp 87.

was at play well before the massive use of computers from the late 1980s, a use that had the effect of modifying many existing working practices towards networking at workplaces.[773]

Many of the cultural features and consequences that these historical changes in production/consumption patterns would have were conceptualised (anticipated) by Guy Debord (1931-1994) in his 'society of the spectacle'. The society of the spectacle refers to developments from the late 1960s where social reality is transformed into a relentless display of images, mainly through advertising, to promote what Debord characterised as an imposed and 'alienated consumption' behaviour.[774] In his view images were constantly detaching from everyday life practices,[775] rendering people increasingly submissive to the 'contemplated object'.[776] Under this regime, he argued, the present became perpetual,[777] devoid of history; as such the spectacle becomes 'out of reach' and above all 'beyond dispute'.[778]

### 6.2. Hyperreality and cell biology: is the map preceding the territory?

For Jean Baudrillard (1929-2007) Debord's ideas on spectacle were just the beginning of a process that would have important consequences for reality itself. An important concept in Baudrillard's work is that of 'precession of simulacra'. This term

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773 See Chapter 3. That to say, that networking practices are not necessarily technologically driven. It is undeniable however that the massive use of computers at different workplaces, the so-called information technology revolution taking place from the 1980s has been instrumental for the creation of networks by allowing the restructuration of work practices towards 'flexible specialisation'.

774 Guy Debord, *The society of the spectacle*, New York, Zone books, 1994, pp 29. (Original edition in French, 1967). Advertising, that is the production of written and/or visual messages directed to audiences suggesting the buying of a product has a long date. In the 1960's however the activity began to diversify and use new methods directed to connect different aspects of the addressee's life. It was noticeable for instance, the construction of a 'symbolic aura' connecting the commodity with other aspects of people life's, desires and dreams. Andrew Wernick, *Promotional culture: Advertising, ideology and symbolic expression*, London, Sage, Publications, 1991. See www.spotlightideas.co.uk/?p=4854 consulted January 2011.

775 Debord, 1994, op. cit., pp. 12.

776 Ibid. pp. 23.

777 Guy Debord, *Commentaires sur la société du spectacle*, Paris Gallimard, 1992, pp 25. (original 1988).

778 Debord, 1994, op. cit., pp. 15.

describes a present condition in our societies, which is based on a logic of simulation, a logic where the representation substitute the real, in other words a logic where the real is taken to be its representation.[779] He uses a short fable from Jorge Luis Borges (1899-1986) 'Of exactitude in Science' where an emperor commands the making of a map that becomes so detailed that it finishes by having the same size as his kingdom, being impossible to distinguish which is which. Baudrillard states: 'It is not the territory that precedes the map but the map that precedes the territory'. In other words, he makes the case for the way representations in our current time are concealing the absence of reality, or at least of the kind of reality that we take for granted.[780] Reality has either 'imploded' or has been 'perfectly murdered', leaving no trace, so that 'in our virtual world, the question of the real, of the referent, of the subject and its object, can no longer be posed'.[781] He uses the term hyperreality to refer to this visual world where simulations abound and where signs, images, representations, presentations and models are relentlessly produced and circulate, detached from any material object. This 'logic of simulation' is so pervasive, Baudrillard argues, that once born, it has remained as the main organizing principle in these societies.

In his view, this condition of hyperreality where images of objects conceal their materiality corresponds to the latest form of the history of the sign in our societies. So Baudrillard goes further than describing that present condition and attempts to historicize the nature of 'representation' throughout the history of western societies. For that he uses the concept of 'orders of simulacra'.[782] He divides the history of the sign after the classical era (the era in which signs pointed to a material or social reality, with a signifier associated to a signified in an indexical fashion), in three successive stages of simulation: the counterfeit order, the order of production and the present order of simulation. The order of counterfeit, which ran from the Renaissance to the Industrial revolution, was characterised by imitation and an indexical relationship between signifier and signified.

779 Baudrillard, 1994, op cit., pp. 1-42. Also viewed as a growth of symbolic over iconic forms.

780 Ibid. pp. 1. Or at least of what we consider it to be so far (see discussion below).

781 Jean Baudrillard, *The vital illusion*, New York, Columbia University Press, 2000, pp 58-83.

782 Baudrillard, 1993, op. cit., pp. 50-86.

Objects reproduced were considered as being copies of an original and hence a clear difference was made between semblance and/or representation and 'reality'. The order of production, the dominating period during the industrial era, was characterised by illusion and involved indirect signifier/signified links, with images viewed as reproductions of objects with the relation between them as one of equivalence. Finally, the order of simulation, the one that characterises our current era is characterised by a relentless emergence of signifiers that are temporarily linked to signifieds. Reality becomes possible through its reproductions, no matter its link with material referents. In the order of simulation the relation between referent and sign, between reality and its representation blurs. One important aspect to notice from Baudrillard's orders of simulacra is that from the order of counterfeit onwards the link between signifiers and signifieds weakened and that this arguably corresponds to a move from an indexical/iconic forms towards a symbolic one, as I am proposing for cell biology from the 1980s.

Having introduced Baudrillard's ideas, it is time now to discuss why they are relevant for the visual change in cell biology that this dissertation studies. Let us start by examining the possible relationship between Baudrillard's 'orders of simulacra' and the main characteristics of the microscopical and molecular imageries. Although it is difficult to establish a point-by-point relationship between each kind of imagery and Baudrillard's orders' especially in their temporal association, the following relations could, in my opinion be established. Optical microscopical imagery possesses some aspects of the 'counterfeit order', for images of cells, especially those obtained with an optical microscope, are conceptualised by its producers as reproductions. That is, microscopists take an image of a cell rendered by an optical microscope as a copy of an original, which is mounted on a slide. Electronic images of cells, without losing the above-mentioned characteristics for optical imagery, possess in addition some of those features that Baudrillard ascribes to the 'order of production'. As I argued in Chapter 4, electromicrographs are indexical signs because of the way they are connected to the object, the cell, through the optical image. This is in line with the relation of equivalence between object and image that the 'order of production' prescribes (as equivalent elements in a series of identical objects). Finally, concerning the last of Baudrillard's

orders of simulacra, that of the 'order of simulation', it is my contention that molecular imagery bears some resemblance to this order, not only because, as this order suggests, cells get defined through the possibility of an equivalent reproduction, but because its very reproduction erases the cell as a referent.

What about the relation between Baudrillard's last order of simulacra that of simulation, and the visual change in cell biology? In considering our above discussion and the conclusions from the semiotic analysis of microscopical and molecular imageries (Chapter 4) it seems reasonable that a parallel could be established between the relentless proliferation of signs in cell biology as a result of the latest wave of molecularisation of the discipline, and Baudrillard's characterisation of our present condition of hyperreality in modern Western societies. In my view, when analysing the proliferation of images on signal transduction and interactomics it is unavoidable to think of Baudrillard's thoughts of a relentless proliferation of simulations referring only to themselves with the resultant erasure of the real, or at least of the real as we know it.

Critics have argued that Baudrillard's perspective is not new and what it does is only to reiterate two classical themes from the western tradition of philosophy,[783] namely the possibility of access to the 'real' and that of choice between alternative representations/presentations of the same referent. For the case of cell biology these themes take the form of what we take a 'real' cell to be like (as defined by the microscopical or the molecular image) and how we judge the reliability of a representation/presentation if we have problems in judging the relationship of the sign to the referent (especially through history).

A widespread view in science is to believe that any latest expression, visual or epistemic, constitutes a better approximation to what the system under analysis is- in our case, that molecular imagery delivers a better (a more real) picture of what cells are, and

783 As Giles Deleuze has pointed out, themes on reality and simulation have a long history, as Plato's writings on the cave suggest. Cited in Michael W Smith, *Reading simulacra: Fatal theories of postmodernity*, New York, Albany, State University of New York, 2002, pp. 5. The point is that perhaps the very nature of the relation between reality and its representation/presentation is always blurred and hence problematic.

above all, do. In the context of this work I decline to take either a microscopical or a molecular image of a cell as more 'real' than the other. This is because, as argued previously (Chapter 4), the microscopical and the molecular are in fact two (related) but different ways of 'world making', each having their own methodologies, codes and rules for consistency, and as such, each serving to emphasise different aspects of cells. Neither the microscopical nor the molecular has any privilege of accessibility to the cell, each of them in fact deals with it in different ways. This is something that becomes concealed from view because of the idea that there is a presumed dichotomy between the real and the virtual, a dichotomy based on the assumption that what is real exists and what is virtual belongs to the realm of fiction.[784] The limitations of this view where highlighted by Manuel Castells, who is of the opinion that, 'reality as experience has always been virtual because it has always been perceived through symbols which entail some meanings that escape their strict semantic definition'.[785] My argument on non-privileged forms of representation/presentation is further substantiated by the work of Lynch on representations in science.[786] He argues that there is no way to compare a representation of a biological phenomenon to the 'real thing' since the latter becomes coherently visible only as a function of representational work, an assertion that of course does not entail that representations are complete fantasies. To some extent, these positions are close to the one adopted by Baudrillard himself in his orders of simulacra, who characterises the real as 'that of which it is possible to provide an equivalent reproduction'.[787]

Another factor contributing to the progressive view of representations/presentations is that seeing as attainable the creation of a global and totalising (real) vision of a cell, out of the contribution of both imageries. Without denying that the complementary use of both imageries may be productive for the intelligibility of cells, a global image of them as a consequence of the combination of both imageries seems to be unattainable. As the art critic James Elkin has pointed out, the

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784 Fiction (as symbolism) being a forbidden word in the lexicon of science.

785 Castells, 1996, op. cit., pp. 372.

786 Michael Lynch, Science in the age of mechanical reproduction: Moral and epistemic relations between diagrams and photographs, *Biology and Philosophy*, 1991, 6: 205-26.

787 Baudrillard, 1993, op. cit., pp. 73.

search for a comprehensive image of entities at the verge of the 'un-representable' (he refers to viruses), no matter the number of depictions from different origins produced, would always be incomplete, not fully realised.[788] This condition of incompleteness, he argues, arises because the different viral 'representations', which rely on different pictorial strategies (each involving different symbols, surrogate forms and visual metaphors), 'cannot (because of their incompatibilities) be fused in a single whole image'.[789]

From all these considerations then, this dissertation takes the view that each system of 'representation/presentation' creates its own reality and that there is not an original real cell to which to compare the different representations or presentations of them that have emerged historically. Wilson's cells are/were as real as those portrayed in CB or in MBC. The only difference among them is to be found in the following. From the time of cell theory to the late 1970s there was still an idea of the 'real' close to the one sustained by Baudrillard in his order of production, one in which it was possible to give an equivalent reproduction of a cell. From the early 1980s however all this changed with the development of the third-generation models of molecular imagery especially with the explosion of models on signal transduction pathways. Cells defined by the molecular paradigm doubles (duplicates) the 'real' and with this a substitution of realities emerges.

The discussion in this dissertation of issues of reality and hyperreality in cell biology aims to encourage reflections on the capacity of an experimental practice based on molecular imagery to operate in the 'real' world.[790] An issue that could be encapsulated in the following question: how effective is this imagery to 'fix' diseases?

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788 James Elkins, 'Art history and images that are not art'. *Art Bulletin* Vol LXXVII. Number, 1995, 553-571. Pp 568-569. Elkins discuss the work of Stephen Harrison on viral structure where ten different depictions of viruses are shown. Harrison, Stephen. (1991), 'What do viruses look like' The Harvey lectures LXXXV 127-152, esp 128.

789 Ibid.

790 By operational I refer to the capacity of models to produce changes in the world of a different nature than creating new experimental conditions. In other words operational at the level of their alleged capacity to 'cure diseases'.

Or, how relevant is that map that precedes the territory for these conditions? Without denying the importance of this imagery for the sustainability of experimentation, its self-referential character, is becoming problematic. This self-referentiality, viewed as complexity, is deeply concerning its producers. As previously discussed in Chapter 3, Martin Raff, conceded that the growth of signal transduction imagery was going somehow out of control threatening the very process of intelligibility of cells. Moreover, recently some cell biologists and writers have recognised a sort of critical state of the latest form of molecular imagery. Viewed as an excess of complexity, these concerns started to crop up in the editorials and comments sections of scientific journals. The editorial of a special issue of *Science* on signal transduction, for instance, acknowledges that the level of intricacy achieved in the field is worrisome. It states that 'The pathways are lengthening and the growing alphabet soup of acronyms make it difficult for even those in the discipline to keep up […] It is a challenge for us at *Science* to edit the abstracts and titles of papers in this field, so than others can understand them.[791]

Another example is that of Jonathan Slack, a developmental biologist, who in his recent review of the latest Fox-Keller's book states that:

> She (Fox-Keller), does not include a discussion of what is really worrying many molecular biologists: the vast mass of genetic and molecular data that is being generated in the post-genomic era and the apparent impossibility of organising all the material collected into any manageable type of explanation.[792]

One of the most visible consequences of the growth of molecular imagery has been the almost exclusive trust given to molecular models not only to explain diseases but also to cure them. One of the results of the visual change has been in my view the neglect of the cellular model. As the figures in **Graph 2** (see page 117) suggests, images of cellular models in MBC between 1983 and 2008 represented between a 7.42 and a 5.47% of the total amount of images contained in the textbook (an almost 2% decline), compared with the images of third-generation, which increased from 10.45 to 30.85%, (a 20.40% growth) in the same period. A related and genuine concern about the decline of the cellular model and the capacity of the molecular ones to explain the inner workings of

791 Donald Kennedy, Signals ahoy!, *Science*, 2002, 296: 1569.

792 Jonathan Slack, What is an explanation?, *Science*, 297, 1813.

the cell in complex phenomena like asthma has been recently highlighted by Persson and his colleagues.[793] They argue that in a 'molecular-biology-driven imbalance, several inflammatory mechanisms (allegedly related to asthma and allergic rhinitis among others), now under intense investigation molecularly *in vitro* and in mice, might not occur in human tissues in vivo'. This is of particular relevance when considering that some of the images carrying models for developmental pathways, for instance, despite being incorporated in textbooks are not necessarily those sustained by the 'most solid' experimental data that the peer reviewing process considers to be valid.[794]

The point I am trying to bring our attention to concerns the perils of blindly positing too much confidence into a system that seems to be producing too many signs and symbols, and which is hard to conceptualise into a reasonable operational system to control disease. The case that this dissertation argues for is to avoid an unnecessary exposure of molecular imagery as a symbolic non-sense imagery and equally to avoid positing too much confidence on it at the instrumental level, a confidence that may hamper and discredit the deployment of those technologies.[795]

A recent paper alerts us to the caution that scientists should have when displaying images of symbolic nature because of the 'illusory' condition these images may create by making opaque the reality/appearance distinction.[796] As Pitt succinctly put it: 'Never underestimate the ability of human beings for self delusion'.[797] Much in line with the arguments developed in chapter 4 of this dissertation, Pitt argues that electron

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793 Carl G A Persson, Jonas S Erjefalt, Lena Uller, Morgan Anderosn and Lennart Greiff, Unbalanced research, *TRENDS in Pharmacological Sciences*, 22: 538-41.

794 Michael W Klimkowsky, 'Minireviews, minidogmas and mythinformation', *BioEssays,* 1997, 19: 537-9.

795 It has been recently argued that in the 19th century pathologists started to analyse microphotographs instead of analysing the microscopic specimens themselves as a consequence of positing the mechanical reproduction as a substitute of the 'real' specimen. This began to discredit the use of microphotography for a while, only to be rehabilitated around the 1880's when R Koch (1843-1910) made microphotography central to microbiology. Breidbach, 2002, op. cit.

796 Pitt, 2005, op. cit.

797 Ibid. pp. 30.

microscopic and nanotechnology so-called images are not images because they are not representational, that is, they are not based on resemblance. In Pitt's view an image is not an image when: 'we do not know if it is representational but conveys information none-the-less'.[798] However, because these images convey information in a visual format they create a problem of how to determine their purported level of accuracy. Electron microscope and nanotech images are 'heuristic imaginings', which are based on extended metaphors of the concept of seeing.[799] The use of extended metaphor is essential to erase the complex interpretative process, at play when seeing 'through instruments' and hence to create the illusion of making the unknown easily approachable. This last point, take us into Pitt's normative and ethical arguments concerning the use of symbolic imagery in the sciences, arguments that in my view need to be taken into account. In his view scientists are misleading the public when they fail to disclose how the computer-enhanced electron microscopic images of the nano-world are made.[800] Pitt's point is that this type of image, which is no more than a 'beautiful simulation' resulting from overloaded decisions including codes and conventions introduced in the imaging software, raises false expectations by giving the impression that we do know more than we really do and hence that we can do more than we really can.[801]

The condition that both some scientists and some members of public fall into is one of unconditional adoration of this imagery because, Pitt argues, it makes everybody believe that the 'nanoworld' is a tangible and simple place. However, as quantum mechanics has taught us, 'the microworld' is fuzzy, pemanently 'buzzing', 'shifting' and constantly changing its motion in a 'non-linear and non-classical causal fashion'.[802] So, the image of the nano-world as a simple and easily manoeuvrable one is not only misleading, but epistemologically suspect. In fact, to ask public acceptance of the nanotech imagery in his view is too much, especially on occasions when a treatment for a

798 Ibid. pp. 27.

799 Ibid. pp. 31.

800 Ibid. pp. 30.

801 Ibid. pp. 31.

802 Ibid. pp. 30.

given disease does not work and explanations for the failure involve phrases like: 'well it is more complicated than that', once you have previously created insubstantial expectations on an imagery that 'presents' the realm of the minute as a simple and straightforward place.[803]

I would like to end this chapter with the following questions. Are images of a molecular nature acting as an end in-themselves within the cell biologist' work? Are they only visual commodities getting more and more distanced from the real world from where they have emerged? Are the new visual producing technologies giving us the illusion of control over it?[804] George Canguilhem expressed these questions as deep concerns. [805] He thought that twentieth-century biology was fascinated by the prestige of the physico-chemical sciences and consequently it was reducing itself to a satellite of these. Such a reductionistic biology, he remarked, implies as a corollary the disappearance of the biological object as such. Canguilhem, although from a different perspective to that of Baudrillard, was somehow anticipating the possible consequences of the relentless growth of visual forms in science, and cell biology in particular.

Only time will tell whether the growth of the latest visual form of molecular imagery, in other words, the move from representation to presentation in cell biology has created a condition of hyperreality where the difference between what is taken to be real and what is not no longer holds, a condition that may negatively affect the highly praised operational capacity given to pictorial representations in science by its practitioners.

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803 Ibid. pp. 31.

804 Modified from Baudrillard. Jean Baudrillard, *The perfect crime*, 2008, London, Verso, pp. 5. (original in French Le crime perfect, Paris Galilee, 1995).

805 George Canguilhem, *La connaisance de la vie*, Paris, Vrin, 1965, pp. 83.

**Conclusion/Discussion.**

This dissertation has analysed a visual change that occurred in the discipline of cell biology during the period 1950s-2000s. An examination of the images contained in cell biology textbooks during the period 1940s–2000s, has revealed that the number of images of a molecular nature has come to outnumber those of a microscopical nature. This examination has also revealed that two overlapping but different epistemic traditions, the microscopical and the molecular, have constructed the visuality of cells. The scientific selves responsible for these epistemic cultures in their pursuit of creating knowledge on cells, have displayed a distinctive repertoire of moral codes for the setting of the standards of the technologies under use for the realisation of the main epistemic objectives of the discipline.

The kind of molecular imagery that this study describes (dubbed as 3rd generation) as emerging (late 1970) and ending by displacing (early 1990) the microscopical constitutes the visual embodiment of the latest phase of a process that scholars have dubbed, the molecularisation of biology.[806] The main characteristic of the visual form of molecular imagery (its latest), the one that sets it apart from its previous forms, is its intimate association with cellular process, an association that has ended by eclipsing the central role traditionally assigned by the microscopical culture to the cell in biological processes.

This growth of molecular imagery and the subsequent establishment of a current visual regime based on it has had major consequences for the research agenda of cell biology. It has, for instance, not only changed what is in need of explanation, but fundamentally how it is explained.[807] Thus, during the period under analysis (1940s-2000s) the explanation of cellular phenomena, such as migration, differentiation and so forth would shift from cells themselves towards molecules. This explanatory shift entailed also a direct connection being made between functions and molecules and with it

806 Abir-Am, 2003, op. cit. de Chadarevian, et al. 1998, op. cit. Kay, 1993, op. cit.

807 Michel Morange, *Les Secrets du vivant: Contre la pensée unique en biologie*, Paris, Editions La Découverte, 2005. Microscopical and molecular epistemic cultures could be seen as different sub-disciplines.

a consequential devaluation of the role of cells in these processes.[808] Concomitant to this change in cell biology in what is need of explanation and how it is explained the latest inroad of molecular culture into the discipline from the mid 1970s provoked two important changes in the nature of its research. Biological research began to be increasingly driven by 'the experimental system', rather than by theory,[809] a situation that as the following statement from Bruce Alberts, the first author of MBC, suggests, many molecular oriented scientists were aware of.

> This shock, coming after four years of research, forced a complete rethinking of my approach to science […] In the end, I decided to try to develop a method that would provide important new information independent of any theory: I would try to make a chromatography column out of DNA. This DNA-affinity column would hopefully attract all the many proteins in a crude cell extract that normally bind to chromosomes, allowing me to purify these proteins away from the vast excess of other proteins that function elsewhere in the cell. Studies of subsets of these purified proteins might then lead to a detailed understanding of genetic mechanisms, independent of any speculative theories.[810]

Added to this scenario of research being driven by the experimental system, a a related and relevant conceptual change took place in cell biology from forms of intelligibility with their stress on understanding towards forms of instrumental efficacy oriented to the production of effects in cells, but above all oriented towards the production of new phenomena through the experimental system.[811] The visual change described in this dissertation was thus instrumental in producing new cartographies of experimentation steered at designing and controlling cells and with it life itself.[812] With

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808 A process that was, arguably, more resisted by developmental biologists than by cell biologists.

809 Hans-Jörg Rheinberger, *An epistemology of the concrete: Twentieth century histories of life*, Durham, London , Duke University Press, 2010, pp xiii.

810 Alberts, 2003, op. cit., pp. 429-34, on p. 430-1.

811 Peter Dear, *The intelligibility of nature: How science makes sense of the world*, Chicago, London, The University of Chicago Press, 2006.

812 Kay, 1996, op. cit., pp. 87-100, on p. 95.

this, a new science of cell biology become established from the early 1980s, one concerned with intervention: with 'models for' rather than theory, or 'models of'.[813]

Central for the visual change has been the production of MBC, a textbook deliberately designed to replace former textbooks from the late 1970s early 1980s, which in the view of the authors of MBC, were too microscopically and anatomically based, and hence, offering an outdated vision on cells. I have described this process by using, De Robertis et al, *Cell Biology* (CB) and Alberts et al, *Molecular Biology of the Cell* (MBC), textbooks that belong to the microscopical and the molecular traditions of thought respectively. The analysis of CB has shown that some sort of development of the latest visual form of molecular culture was underway in cell biology well before the appearance of MBC in 1983. This molecularisation was however not enough to displace the dominance of microscopical imagery. Besides, molecular knowledge in the hands of the old cytologists was somehow still to remain subordinated to that of cellular activity as a whole.[814] The molecularisation that finally would override the visual dominance of the microscopical tradition was initiated by the founders of molecular biology in MBC.

MBC not only acted as the main carrier of molecular imagery (especially its latest form), but entailed novelty in its making at different levels, novelties that were very much related to the new moral codes enacted by the scientific selves of molecularisation. The innovation brought by MBC can be summarised in four points: Firstly, MBC was produced by a set of authors practising a new from of novelty-driven, non-hierarchical entrepreneurialism, which was in turn based on the idea of networked practices. These practices hinged on a highly interactive and flexible web of different hubs, such as authors, students, publishers, university lecturers and established scientists working in key laboratories where the latest molecular science was being practiced. As we saw in chapter 3, the making of the book encompassed a highly interactive process not only among its authors who constantly interchanged their writings for suggestions and improvement, but also, among them and all the other actors of the network. Moreover, as

813 Keller, 2000, op. cit.

814 This, despite the incorporation of a 'molecular biologist' as an author and the fact that latest edition of the book was produced after MBC and when molecularisation of cell biology was in it's apogee.

we saw, essential for its production was a market research process alongside a 'hidden networking' of authors, with subject specialists doing far more than just giving the authors suggestions on chapters and images. What is more, the network was active not only for the first edition but also for the updating of every subsequent one. Secondly, during the production of MBC a well-conceived illustration program was in place, one with a special stress on imagery as pivotal for the production of knowledge. As we have seen, although originally developed to reinforce the text, images become almost independent in their capacity to tell a story. Thirdly, and in relation to the previous point, MBC in contrast with CB, gave prominence to well-nuanced stories rather than 'facts' and 'data'. The authors constantly paid cautious attention to the presentation of engaging stories; conceptual accounts carefully constructed by the authors to facilitate the process of understanding for students at a time that as Martin Raff expressed when interviewed, very little was known about many things in cell biology (Chapter 3). In relation to this, as recognised by the authors and as noticed by its reviewers, MBC sometimes displayed as 'gospel in the book', experimental results that were not fully proved, a practice that was almost alien to the scientific selves of the microscopical tradition (from Wilson to De Robertis) who adopted a far more cautious style for the presentation of new findings. Last but not least, one of the key novelties in the making of MBC was its pivotal role for the standardisation of molecular visuality in cell biology. This not only because of the vast audience that it reached after publication but also for the vast audience that its authors co-opted and made participant during its production. Alberts et al, created a massive 'disciplined collective' composed of an enormous group of acknowledged and unacknowledged world-wide collaborators, that by giving images and feedback in many forms and by doing suggested experiments produced an implicit consent on the rightness and hence acceptance of the new molecular imagery.

A semiotic analysis of the main types of images contained in cell biology textbooks (microscopical and molecular) undertaken in this dissertation has served to argue for a change from an iconic modality towards a symbolic one in the discipline. Based on the possibility of a visual comparison between the image and referent, this dissertation proposed a correspondence between the optical, the electronic and the molecular image with icons, indexes and symbols respectively. It was concluded that the

degree of cultural convention required for establishing a link between sign (image) and referent was far more complex for molecular images than for microscopical ones. A key concept that helps to better understand the cultural convention at play in the construction of the latest form of molecular imagery is that of 'translation'.[815] Translation refers to all the steps required to produce and use images, including those at play in the transformation from one kind of inscriptions (visual outputs) into other, alongside the unwritten rules and codes agreed by its producers to be used for their interpretation. Translation of signs is a process that is always at stake when images are involved. However, as we move from icons, throughout indexes towards symbols this process gains in complexity and hence in the number of steps required to justify their respective relations with the referent. When thinking on this, it is important to emphasize that despite the many differences between the three type of images assessed in this study (optical, electronic, molecular) the organising principles and/or metaphors used to epistemologically justify them, that of 'the window into the invisible world' and that of 'the continuity of vision argument' remained the same.

Semiotics' contribution to this study does not end there. It also helped to explain why images of a symbolic nature in cell biology, like those from the third-generation molecular models, persuade, become important, and are taken unquestionably as faithful 'representations' of cells. The concept of 'the trace', that is the permeation of indexicality in signs of an iconic nature, in scientific and medical images from referents that remain invisible but that can be unveiled by a new technology, as it was the case of X-rays and is the case of MRI scans, is pivotal here.[816] By taking this line of thought further I have argued for a sort of embodiment of indexicality and iconicity into the symbolic forms from the latest visual form of molecular imagery that began to emerge in cell biology by the early 1980s. Molecular imagery becomes credible beyond the experimental logic from which it arises because of its capacity to harbour indexical and iconic 'traces'. In other words, images of the molecular culture acquire their status because (with the aid of the continuity of vision argument) they are unconsciously taken to be photography like 'representations' giving the impression that their production is based on resemblance.

815 Pauwels, 2006, op. cit., pp. 7-12.

816 Joly, 2004, op. cit.

Besides, the symbolic nature of the images of the third-generation becomes hidden from view because of precisely this transferability of indexicality/iconicity into the symbolic form. This process, which I have dubbed the 'naturalisation of symbolism', is thus coded in conventions that are hidden from view for non-specialists and specialists alike, albeit for different reasons.

Semiotics has also allowed us to argue for conceptualising molecular images as 'presentations' rather than 'representations'. This position addresses both Michael Lynch's original plea (1994) that representation is 'overrated'[817] and the more recent claim by Daston and Galison on the unsuitability of this term to describe science's latest visual forms, those that in their view articulate descriptive and interventionist elements from artistic and scientific perspectives.[818] Using presentation instead of representation serves not only to emphasize the symbolic nature of molecular imagery renderings, but to highlight that they are, because of their lack of reliance on mimesis, convention-based acts of free invention and creation pretty much unrestricted by the type of scientific criteria arguably at use when selecting hypotheses (see later on the context of justification). Thus, molecular depictions, which are 'presentations', due to the absence of a visible referent, in contrast to microscopical 'representations', could afford to be based in figurative and abstractionist forms. All visual renderings, as van Fraassen put it, reach a given balance among likeness, unlikeness, distortion and the addition of new elements.[819] So, whilst it was (and still is) by and large unacceptable for microscopy-oriented cell biologists when producing their iconic and indexical images to trade freely with unlikeness, distortion and new elements, all these categories, especially, the last one, became essential and hence acceptable for molecular cell biologists when producing their distinctive molecular imagery.[820]

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817 The point made by Lynch is that representation means too many things to too many academics. Lynch, 1994, op. cit.

818 Daston, et al. 2007, op. cit., pp. 363-415.

819 van Fraassen, 2008, op. cit.

820 With the development of image enhancing software and fluorescent techniques in microscopy in the last 20 years, the degree of trade with unlikeness, distortions and new elements at play in microscopical practice is proving difficult to evaluate.

As we have seen, although extensive in art, current discussions on symbolism in science, not least its acceptability as productive signs for the production of new expressions, has been and still is by and large avoided in scientific circles. This is, as we saw, because of the strong historical association between symbolism and religious or secular practices such as psychoanalysis that are considered to be unscientific by many philosophers and scientists. As we have seen this position derives, from the influence of the ideas held by many logicians, mathematicians and physicists who by the end of the 19th century regarded the use of images as subjective, and as such they attempted to dispense with them.[821] Their argument was that images would distort the aims of science, and its pursuit of certainty and objectivity.[822] This sort of 'anti image', 'anti symbolic' stance, although never fully rooted inside biology as a clear and easily identifiable position, has left important imprints, imprints which are still recognisable nowadays.[823]

The above discussion serves to highlight the fact that it would be a mistake to fall into the 'structural objectivity'[824] trap and conclude that symbolism in cell biology is *tout-court* a misleading 'act' for the production of knowledge. As the historian of art James Elkins has put it:

> We should not think that simply because symbols require interpretation, they are somehow less than objective. So long as there are justifiably, intersubjectively agreed upon standards of interpretations, objectivity is not undermined. So although scientific models do not accurately mirror anything in nature, they are capable of affording understanding of what occurs in nature.[825]

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821 'Structural objectivity' was an attempt to cleanse science from subjective and biased input. Daston, et al. 2007, op. cit., pp. 253-307. Chapter five' Structural objectivity'.

822 Daston, et al. 2007, op. cit., pp. 253-307.

823 As we saw, a typical case from the 19th century is that of Bordet's opposition to Ehrlich's depiction of antibodies on the grounds that they were highly speculative and fictitious drawings that could deviate the 'correct' pursuit of knowledge in immunology. Cambrosio, et al. 1993, op. cit.

824 Daston, et al. 2007, op. cit., pp. 253-307. What the authors dub as the possibility of attaining objective knowledge without using images.

825 Elkins, 1995, op. cit.

In a similar vein, it is perfectly possible to refer to things that do not exist (or have a debatable existence), and for this reference to be a productive one for a field of knowledge.[826]

That is to say that symbolism plays a substantial role in science as it does in art. As Rheinberger argues, 'Science viewed from a semiotic perspective, does not escape the constitutive texture of the inner workings of any symbolic system'.[827] This is a view that is confirmed when reflecting on the work of Keith Roberts on molecular imagery, a symbolism without apologies, a symbolism, which is blurred behind the authority given by the indexical and iconic 'traces' that it embodies (as well as the discourse of science) but that is able to create new spaces of representations as well as new conditions for the making of more experiments.

The importance of symbols for humankind in general and knowledge in particular was envisioned by Ernst Cassirer (1874-1945) when he argued that symbolism was humankind's 'own achievement' and that therefore there is nothing outside it.[828] In his view, what matters most is the essentiality of symbolism for meaning making. Concerning this he stated:

> Human knowledge is by its very nature symbolic knowledge. It is this feature, which characterises both its strengths and its limitations. And for symbolic thought it is indispensable to make a sharp distinction, between real and possible, between actual and ideal things. A symbol has no actual existence as a part of the physical world, it has a "meaning".[829]

Cassirer's recognition of the strengths and limitations of symbolic systems is central to a critical assessment of the present condition in cell biology with an impressive growth and

826 Gabriele Contessa, 'Who is afraid of imaginary objects?', in D. Jacquette and N. Griffin (eds.) *Russell vs Meinong: The legacy of 'On Denoting'*, New York, London, Routledge, 2008, pp 248-265.

827 Rheinberger, 1997, op. cit., pp. 104-5.

828 Ernst Cassirer, *An essay on man*, 1944, New Haven, London Yale University Press, pp 25.

829 Cassirer, 1944, op. cit., pp. 57.

display of symbolic forms that, because of its relentless proliferation, seems to be close to Debord's 'spectacle'.

If I was convincing enough at showing that there is some relation between the visual change in cell biology and Baudrillard's writings on hyperreality then it is valid to assume that there is a possibility for symbolic systems to go beyond control, or in other words, to take us into another categorisation of the real that could be not only misleading but instrumentally unproductive. In this regard, I think it is always wise to keep in the back of our minds claims such as those of Pitt. For they alert both producers and consumers of images of the detrimental consequences for science that overconfidence in images of a symbolic non-representational nature may have because of their 'presentation' of the minute sub-cellular world as a simple, straightforwardly reachable and hence easily malleable universe.

So, to sum up on this last discussion, although it is not appropiate to dismiss or reject the view on cells brought about by the latest form of molecular imagery as *tout-court* deceptive, it is perfectly possible and even necessary to be cautious of its possible slippage into a glib visuality. After all, as many social studies of science have shown, there is much more to the production of images in a scientific discipline than epistemic reasons. There are structures of social power promoting their production and use, structures that include complex networks of interests normally conformed by a new population of scientific selves pushing for the epistemic reform of a perceived stagnated field, equipped with new technes and moral styles through academic institutions prone to the acceptance of novelty.[830]

A characteristic aspect of the scientific narrative is the description of new emerging knowledge in a discipline as progressive. In a nutshell, that every latest research development supersedes the former in being 'closer to how things really are' in a given phenomenon under investigation.[831] In our case, to assume that molecular imagery

830 As well as the many biotech companies that promote the use of their products in experimental research.
831 This entails an almost exclusive focus on the techne involved in its production with a neglect of the complex network of interests at play in the process.

because of its newness and technical sophistication is superior to the microscopical in defining what cells are and do.[832]

Two analytical sources however have taught us the importance of resisting this vision of 'constructive progress' supported by the 'members account' perspective, a vision which is quite common in the introductory lines (prefaces and introductions) displayed in cell biology textbooks and scientific articles. On the one hand, as Daston and Galison's *Objectivity* taught us, what counts as a right depiction, rather than being a universal phenomenon, depends on the decision taken by the thought collective of what count as such in an specific historical context and with the technological resources existing in that period. Rather than universal, scientific representations are culturally and historically specific. So even if both imageries contribute in different ways to making 'things visible and accountable',[833] 'presentations' do not simply reflect natural properties, they 'are surfaces in which hidden ideological, metaphysical, cognitive and cultural orders are projected'.[834] On the other hand, as Baudrillard's ideas on the orders of simulacra[835] suggest, the status of what counts as real has changed through time, a situation that as we have seen, has re-actualised old philosophical questions on its attainability. With the microscopical and the molecular we are in the presence of two 'engines of image production' (to use van Fraassen's terminology)[836], each with its own code, technologies and scientific selves, each with its own successes and failures to define cells (see later on ways of world making). Therefore, in concert with Daston and Galison's and Baudrillard's perspectives this dissertation does not consider that either microscopical or molecular imagery possesses a privileged access to reality. An extra reason for this stems from Keirns's analysis of McClintock's imagery showing that making an important epistemic point on a theme that is being visually reshuffled by a

832 In all fairness, these accounts co-exist with others that portray both approaches as co-productive, consequently relying on newness to argue for progress. Moreover, recent developments in microscopy could also be conceptualised as new and sophisticated.

833 Michael Lynch 'The Production of Scientific Images Vision and Re-vision in the History, Philosophy and Sociology of Science', In Pauwels, 2006, op. cit., pp -26-40, on p. 37.

834 In opposition to the view of Lynch on them. (Ibid.).

835 Baudrillard, 1993, op. cit., pp. 50-86.

836 van Fraassen, 2008, op.cit., pp. 100-5.

new epistemic culture, heralding a different culture of practising science and 'viewing', is not enough.[837]

In cell biology, the progressive account relies on the idea of the existence of a unique way of 'world-making',[838] that is, a self-contained and harmonious epistemological and visual way of making sense of what cells are and do, all contained in the universal body of science and its method, and based on different approaches (microscopical, molecular, etc).[839] This account (so entrenched in scientific circles and science popularisation accounts) takes the more technologically driven and the latest of the approaches developed, in our case, the molecular, as the more progressive.[840] This study opposes this view by conceptualising the microscopical and the molecular cultures as two distinct 'ways of world-making', each depending on different processes of translation and having its own ways of trading with likeness, unlikeness, distortion and the addition of new elements. Whereas microscopical images are more resemblance based (representations), and in principle more related to the traditional form of the scientific method (as viewed by scientists) to test their validity, molecular ones are less resemblance based (presentations) and thus with a looser connection to the so understood strict scientific method (see below the discussion on the context of justification). What they have in common is the referent (cells) and a sort of code for the rightness of 'rendering', that is the adjustment and endorsement to particular standards, styles, rules and codes that each sets as acceptable and adequate for its realisation. Right rendering applies to each 'way of world-making' regardless of the employment of elements of

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837 Hence the rejection of the establishment of a visual regime claiming to have a better the access to reality just because it is new and more technologically sophisticated.

838 Nelson Goodman, *Ways of worldmaking*, Indianapolis, Indiana, Hackett Publishing company, 1978. Ways of worldmaking as viewed by Goodman pertain at different realms of knowledge (science/art) and are not necessarily in conflict due to their different rules and styles of fabrication.

839 The scientific method has many forms and its exclusivity to science as well as its uniformity across scientific disciplines is a contested issue. Here we take it as having the following basic functioning: The proposal of an explanation in the form of hypothesis and/or theoretical viewpoint for a given observed phenomenon, followed by the creation of possibilities of experimental test of those hypothesis and theories and agreement in a framework of conditions that allows for the selection of what is going to be a good explanation.

840 Of course this is not the only existing view among cell biologists. Many take both approaches as complementary and consider progress as associated to their combination rather than to any of them in isolation.

mimesis (literalism) and of convention (symbolism). Because of this, it does not make too much sense to strictly compare worldviews and see one as more progressive than the other; what counts more is their own internal consistency, their capacity to be able to define the 'world', and for this to crosstalk with other worldviews.[841] The imageries of the various artistic painting styles in the edifice of art co-exist in art textbooks thanks to the scientific discourse that assumes them as unified. Each however, has its own set of cultures of production and rules on rightness of rendering. Despite the co-existence of both imageries in cell biology textbooks, they are not only presenting alternative explanatory views on cellular issues, but can sometimes change the subject altogether and beyond recognition. What is more, they may even differ in their definition of a particular cellular event. How representative this last case is in cell biology is certainly a question that requires further investigation.

In assessing the process of creation of images of molecular culture, we wondered if they pass through a selective test similar to that proposed for the selection of theories (context of justification). The original idea was that they should at least in principle be able to offer a satisfactory explanation of the phenomena which they describe, that it should show some consistency with the contextual knowledge to which they belong, and that they should be able to predict and create new experimental conditions based on what it proposes, especially in the case of an image of a new mechanism for example.[842] Due to the closeness of these requirements to those agreed for the selection of theories and models, we wondered if these criteria really apply to the case of images and, then if they do, how. It was concluded that a sort of context of justification is still relevant for the production and selection of images in science, albeit implicit and applied in a lax way. Images in general and molecular images in particular, even if they are coherent with a particular epistemological claim on a cellular process and allow for the creation of new experimental conditions, they are never, for instance, tested experimentally as such. It is argued here that molecular images because of their 'conventional' rather than 'mimetic' relation to the referent are similar to artistic expressions and as such less reliant on a strict

841 Goodman, 1978, op. cit., pp. 109-10.

842 These are some of the conditions also applicable to the process of theory choice. See Kuhn, 1977, op. cit., pp. 320-339.

process of justification. This of course is a highly debatable point, in two ways. Firstly, as critics have argued, this idea of context of justification as a solid, infallible and as completely independent from the conditions of discovery is an illusion. Secondly, it could be argued that artistic forms if considered as a different way of world making than science, also contain a kind of context of justification. That said, one point is distinguishable, scientists in contrast with artists are permitted to create and present invisible entities, provided these presentations allow them to modify the realm of the visible. In other words, in science it is fine to adhere to a theory based on the existence of invisible entities like electrons and depict them, providing that ultimately energy from a power station, allegedly transported by them, could be brought into households and produce light.

As a final reflection, it seems that for cell biology, as John Berger suggested for our culture in general, 'the relation between what we see and what we know is never settled'.[843] If such settlement is ever possible what is certain is that it will be culturally and historically specific and depend on an amalgam of interrelated factors, such as the emergence of still new scientific selves, new technologies and above all, upon the need to look at cell biology once again from a different perspective.

843 John Berger, *Ways of seeing*, London, British Broadcast Corporation and Penguin Books, 1972, pp 7.

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# FIGURES and CHARTS

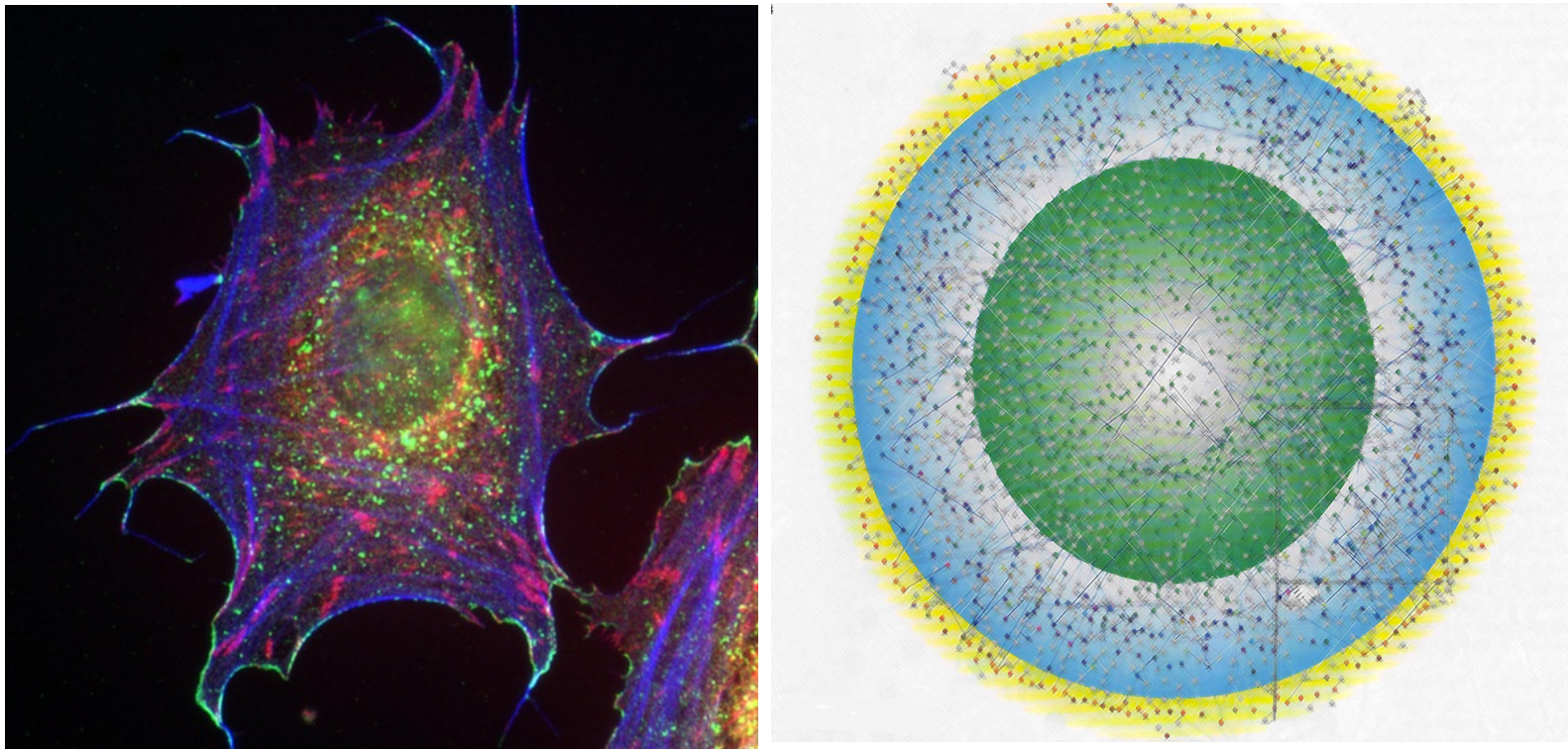


**Figure 1: The Visual Change in Cell Biology: From the microscopic to the molecular image**

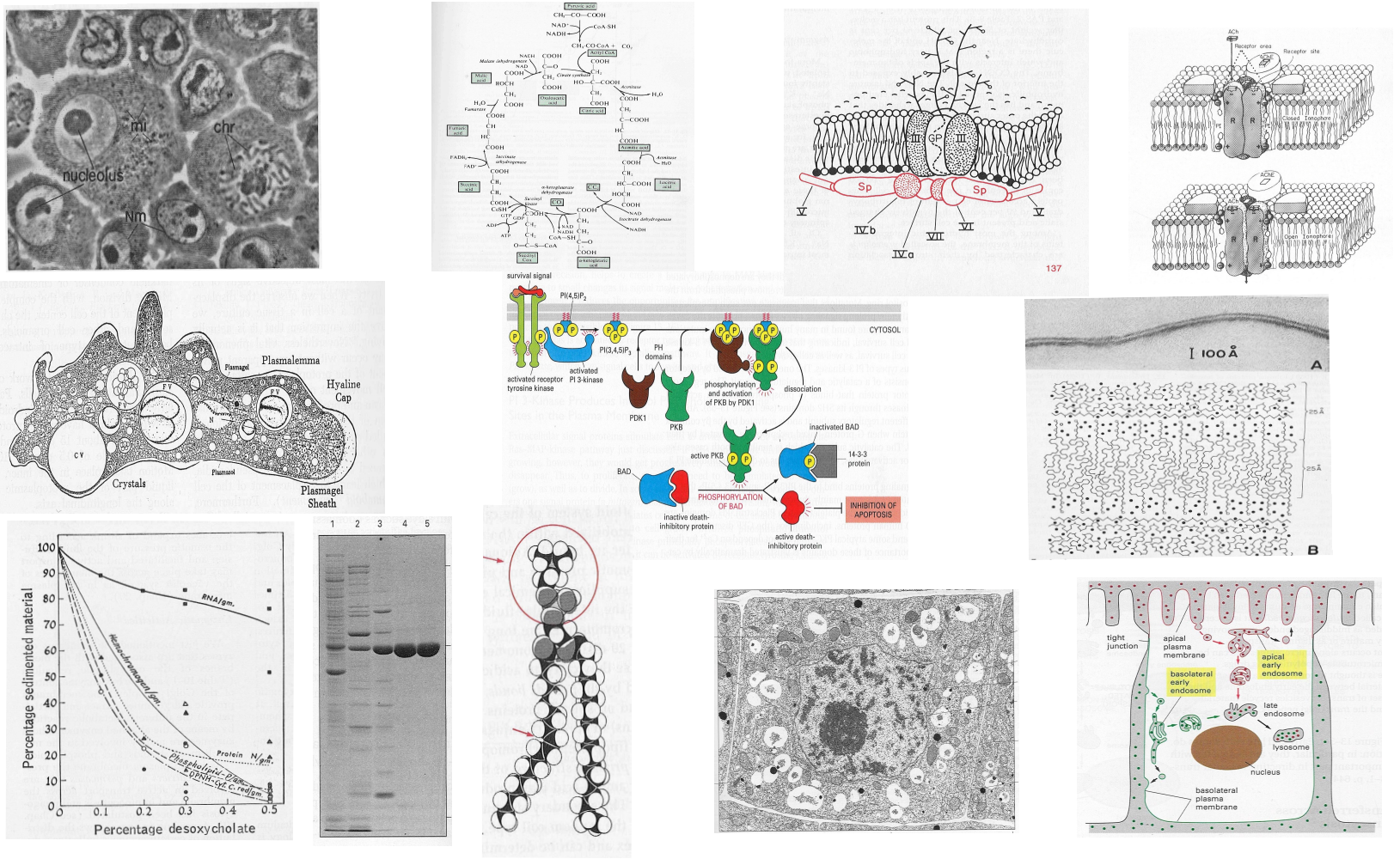
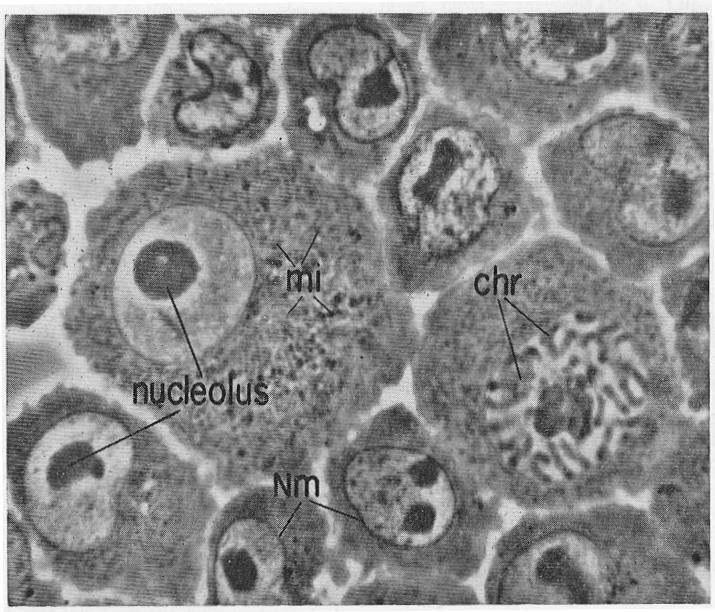



**Figure 2: The different types of images found in cell biology textbooks**

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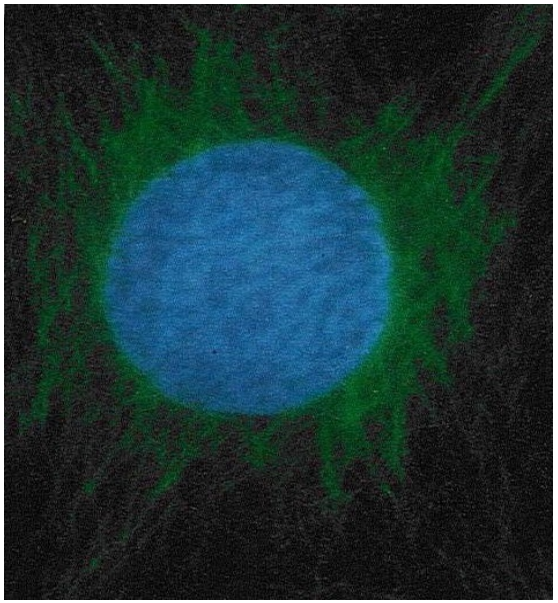


B

**Figure 3: Images of cells or cells components taken with an optical microscope**
**A) De Robertis et al, 1965.B) Alberts et al, 2002**

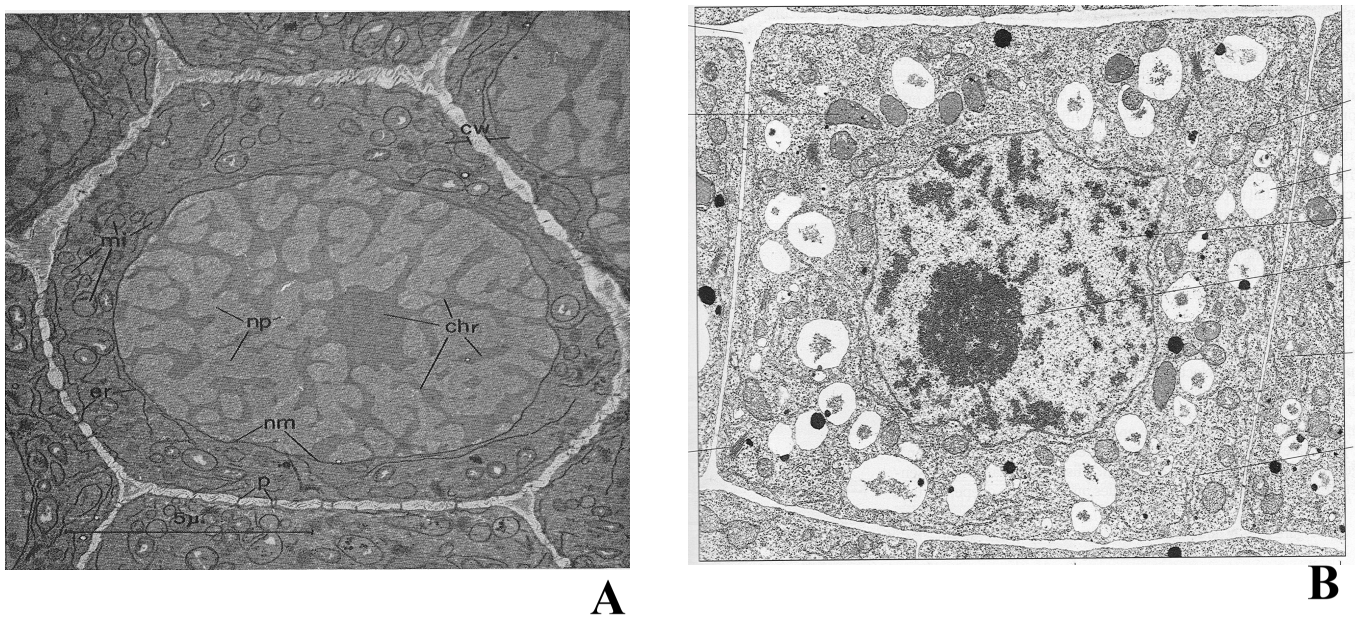
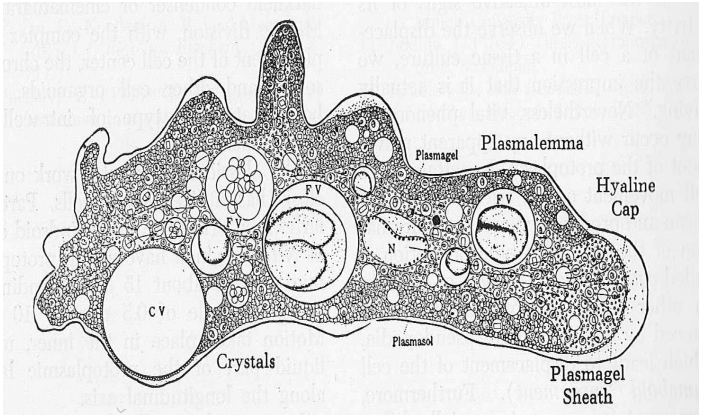



**Figure 4: Images of cells or cells components taken with an electronic microscope. A) De Robertis et al, 1965. B) Alberts et al, 1994**

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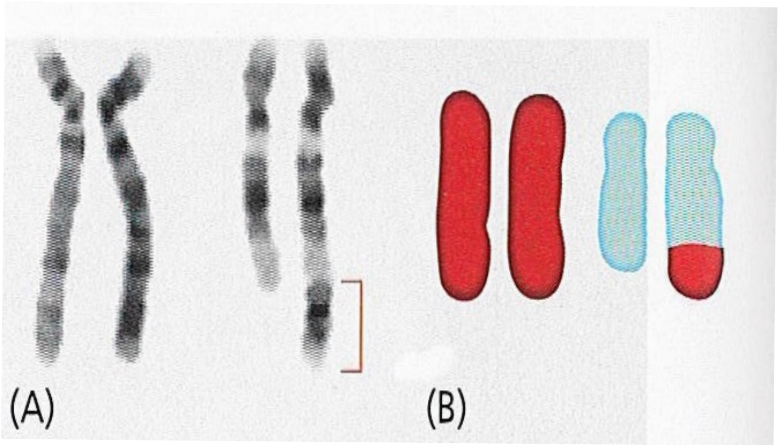
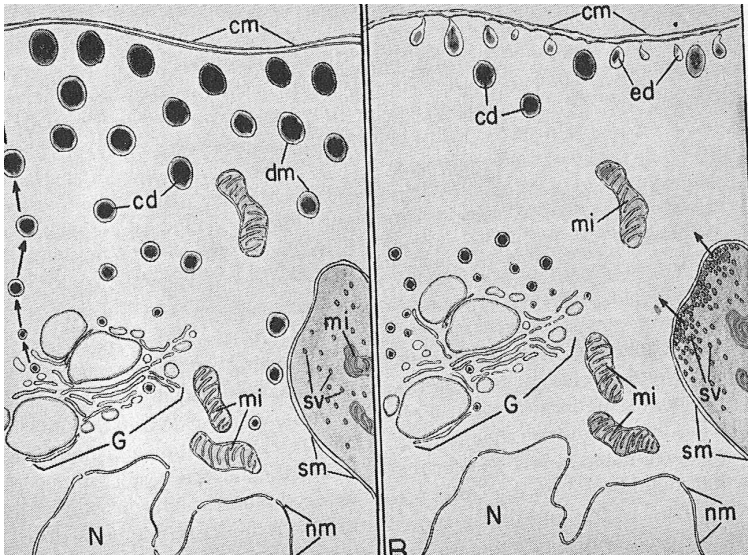


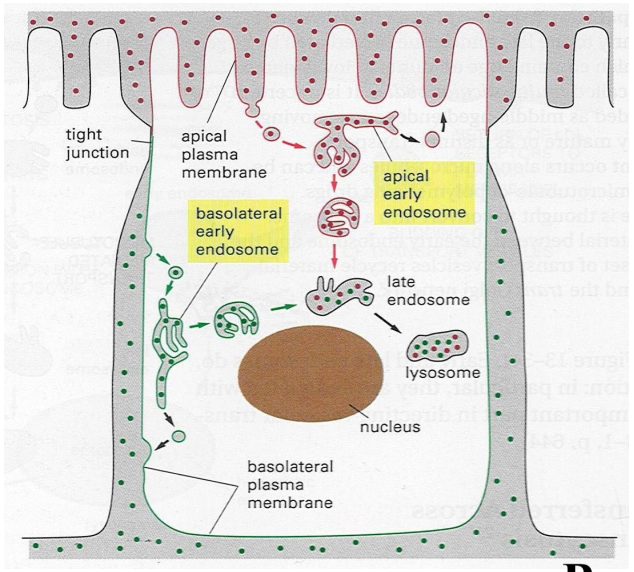

B

**Figure 5: Drawings of cells or cells components (isolated chromosomes, membranes, mitochondria. etc.)**

**A) De Robertis et al, 1965. B) Alberts et al, 2008**

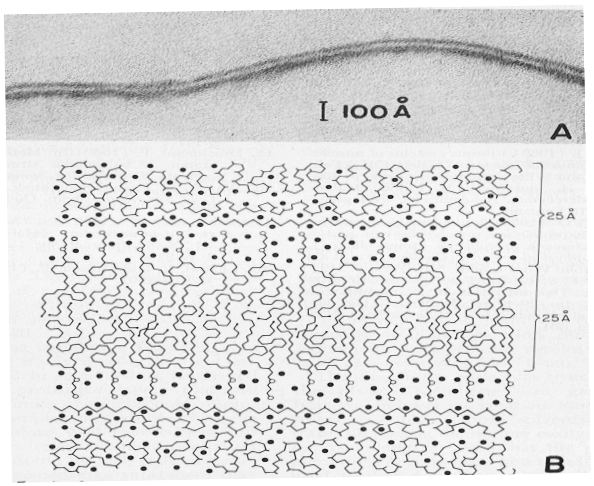



A

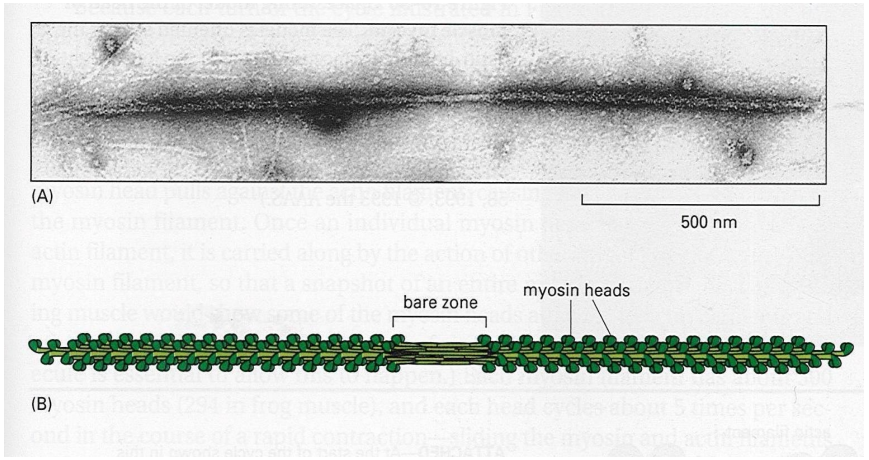



B

**Figure 6: Images of cellular models A) De Robertis et al, 1980. B) Alberts et al, 1994**

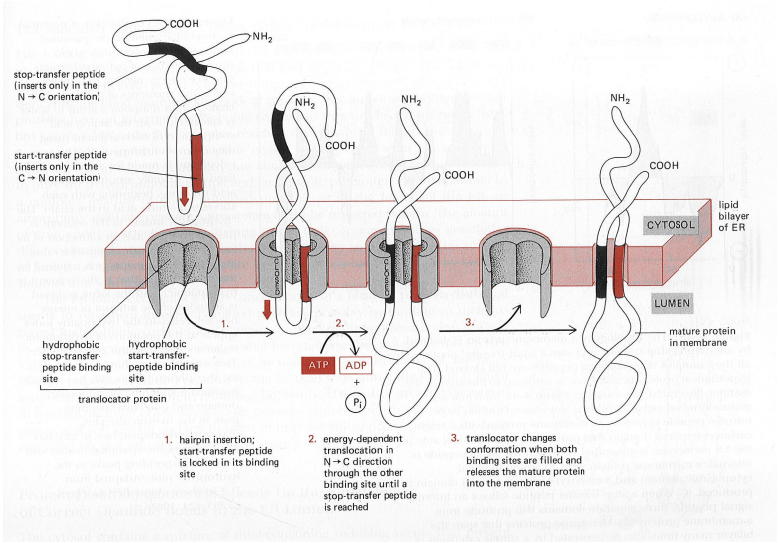


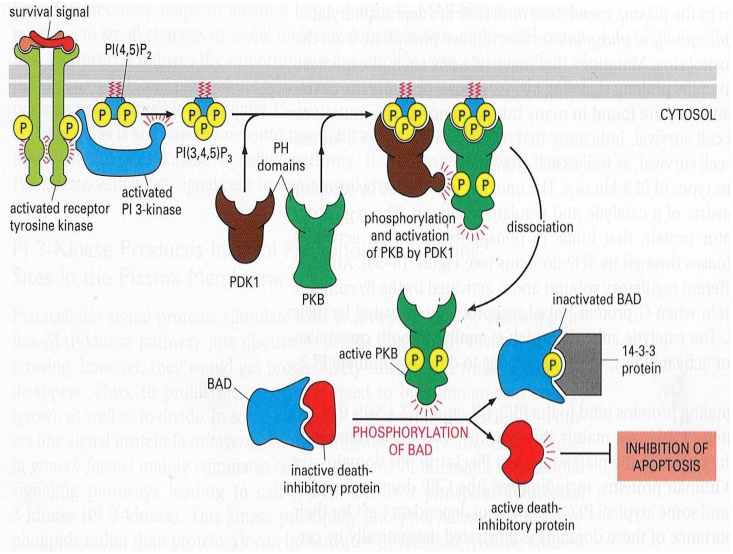

A




B

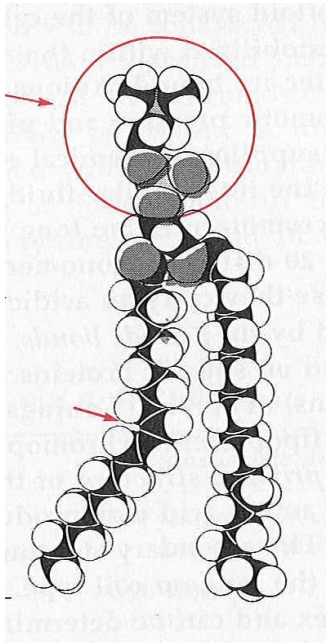
**Figure 7: Models based on images obtained with an electronic microscope.**
**($e^-$ based models: Paired representations) A) De Robertis et al, 1965. B) Alberts et al, 1994**

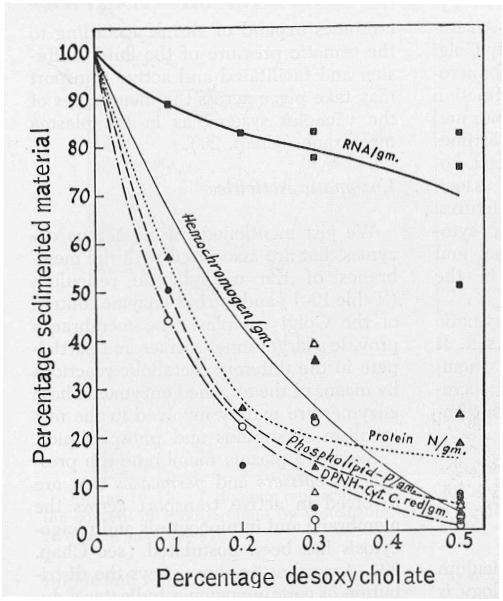


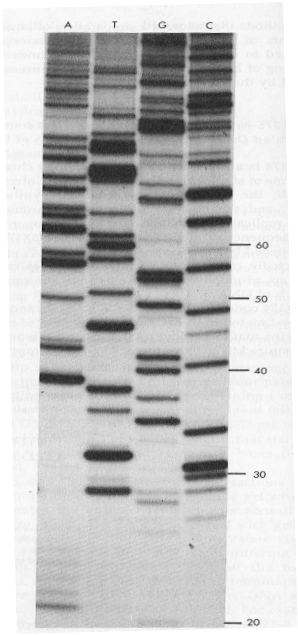




**A** **B**

**Figure 8: Molecular models belonging to the molecular culture (3rd generation models second order) A) Alberts, et al 1986 and B ) Alberts, et al 2002**






**A** **B** **C**

**Figure 9: All other pictorial forms: A) molecules (1st and 2nd generation models molecular culture, B) diagrams, charts. C) gels, apparatuses etc.**
**A) De Robertis et al, 1980. B) De Robertis et al, 1965. C) De Robertis et al, 1980**

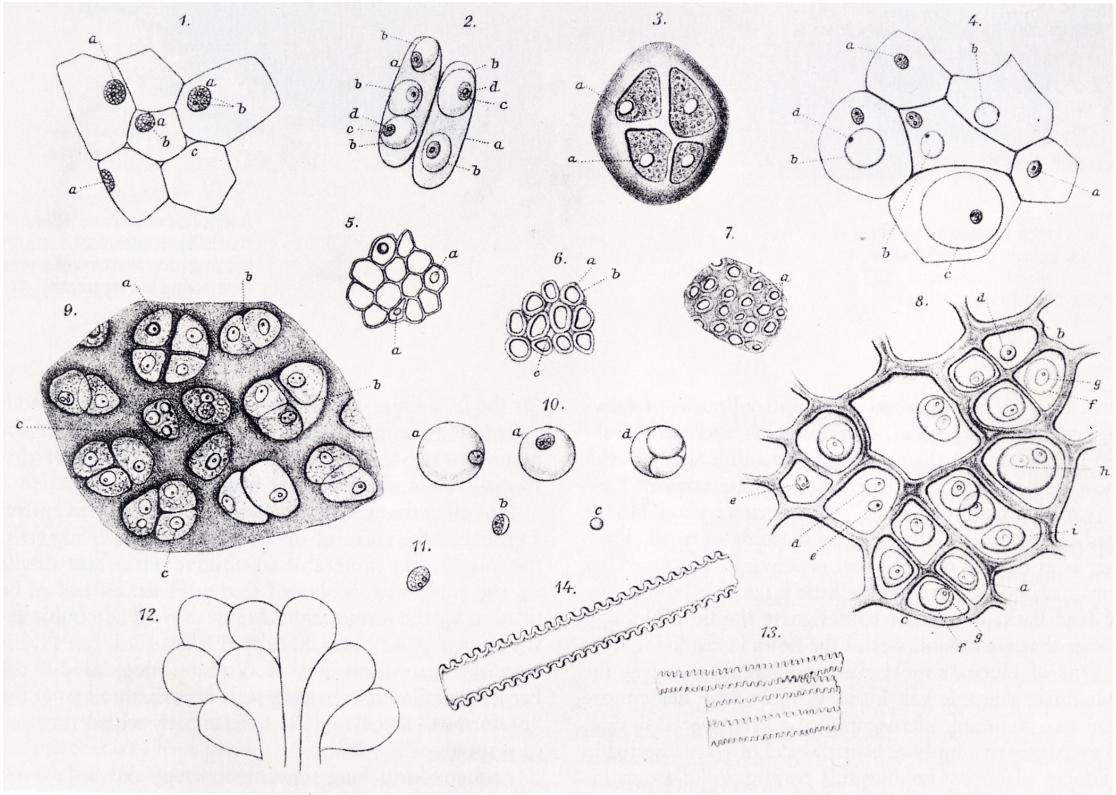
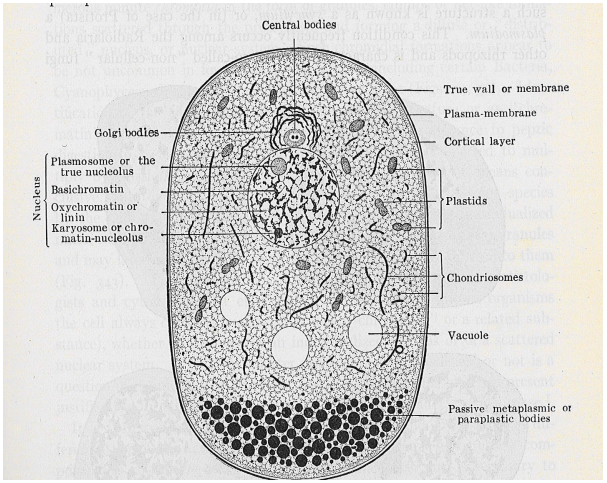
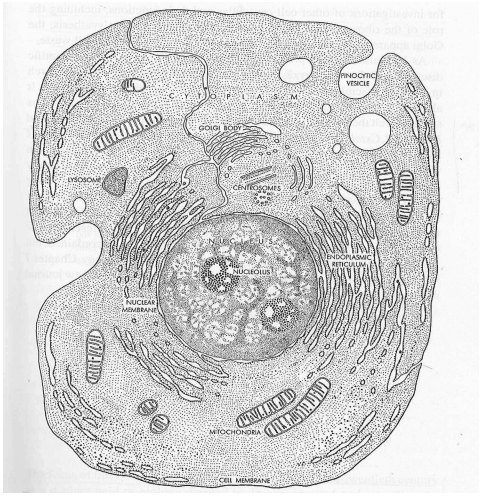


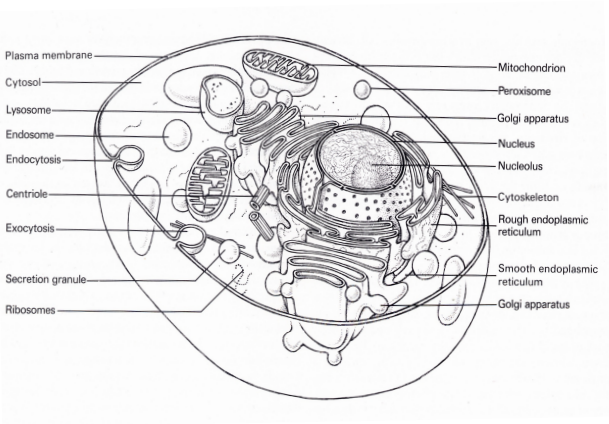
**Figure 10: Schwann drawings of different cell types, Schwann, 1839-1847**




A




B




C

**Figure 11: The Ideal Cell type. A) Wilson, 1925 B) Brachet, 1961, C) De Duve, 1984**

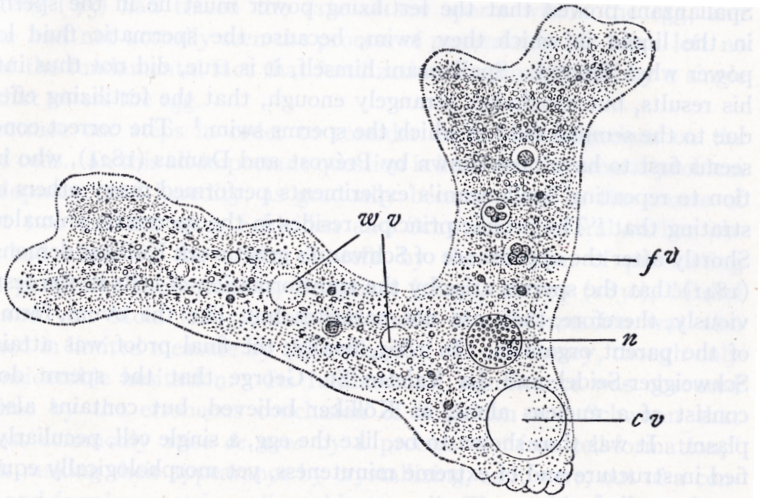



**Fig. 3.**—*Amœba Proteus*, an animal consisting of a single naked cell, × 280. (From Sedgwick and Wilson's Biology.)
*n*. The nucleus; *w*. *v*. Water-vacuoles; *c*. *v*. Contractile vacuole; *f*. *v*. Food-vacuole.

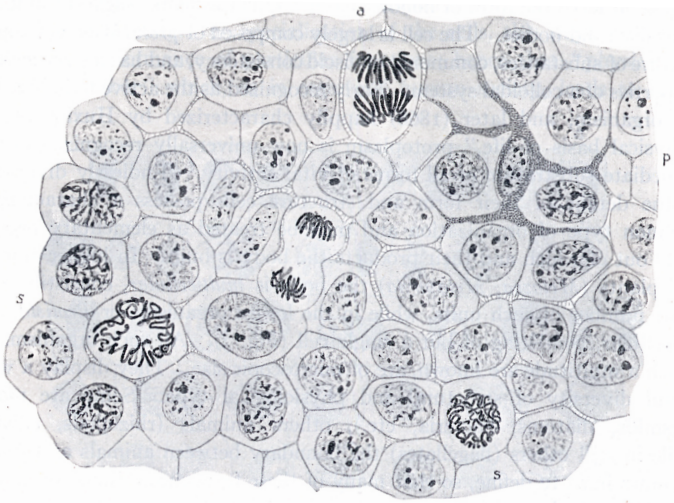



**Fig. 1.**—A small portion of the epidermis of a larval salamander (*Amblystoma*) seen in a slightly oblique tangential section, enlarged about 550 diameters. Most of the cells, polygonal in form, are in the so-called "resting" or vegetative (non-mitotic) state; but several are undergoing division (mitosis). Near *s* and *s* are spireme stages of mitosis, near *a* a middle anaphase, and near the center a late anaphase. Near *p* is a branching, granular pigment-cell that has crept up from below, forcing its way between the epidermal cells. Note the delicate plasma-bridges (plasmodesms) by which the latter are in many places connected. (This figure is combined from three separate camera drawings.)

**Figure 12: The contrasting imagery of the cytoplasm (left) and the cell nucleus (right) Wilson, 1925**

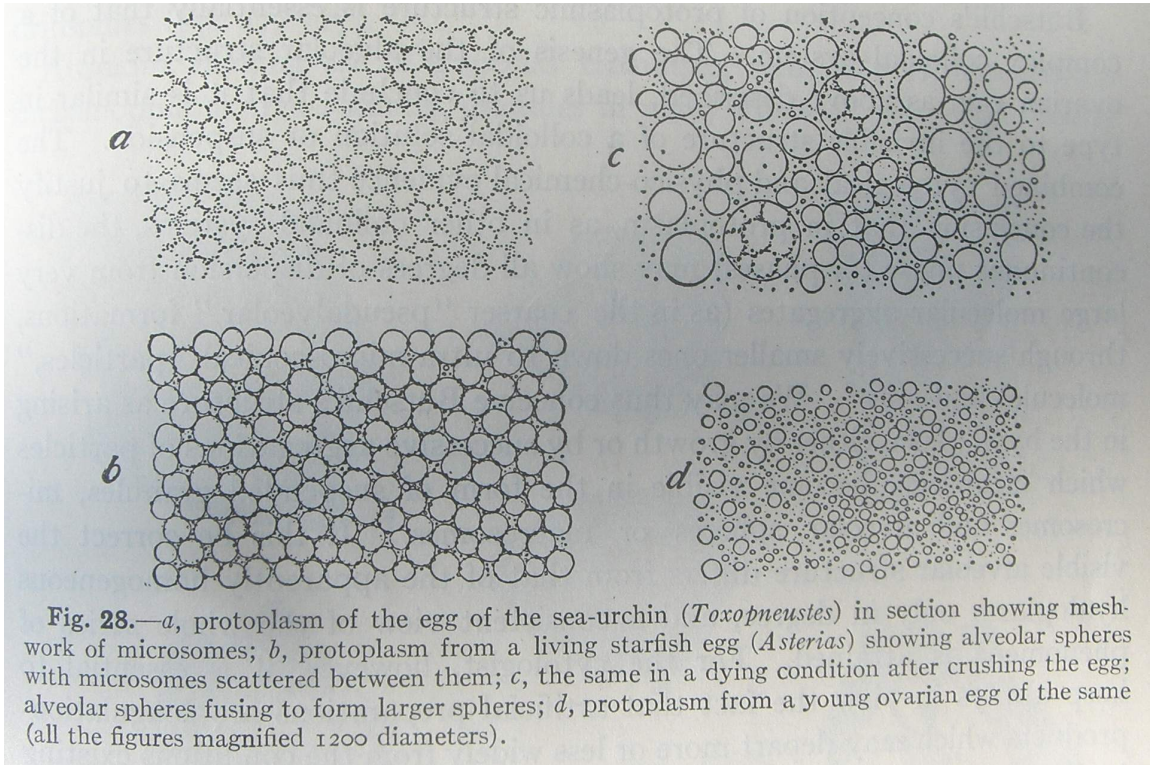



Fig. 28.—*a*, protoplasm of the egg of the sea-urchin (*Toxopneustes*) in section showing meshwork of microsomes; *b*, protoplasm from a living starfish egg (*Asterias*) showing alveolar spheres with microsomes scattered between them; *c*, the same in a dying condition after crushing the egg; alveolar spheres fusing to form larger spheres; *d*, protoplasm from a young ovarian egg of the same (all the figures magnified 1200 diameters).

**Figure 13: 1920s images of the cytoplasm. Wilson, 1925**

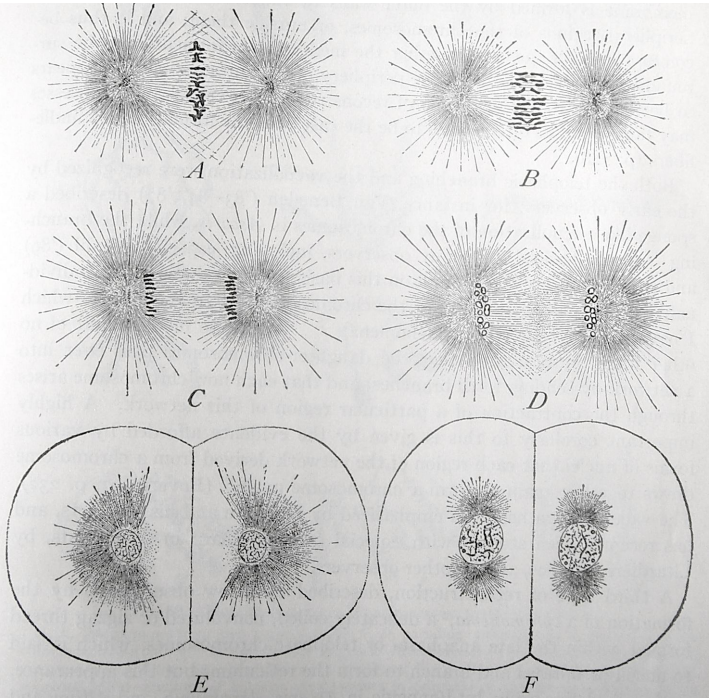



**Fig. 58.**—The later stages of mitosis in the egg of the sea-urchin, *Toxopneustes* (*A–D*, ×1000; *E–F*, ×500).

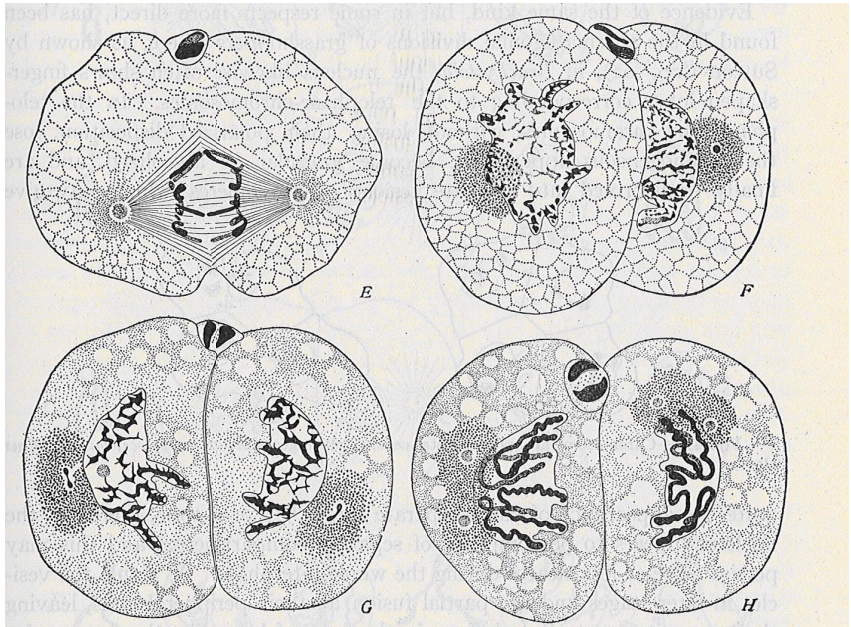



**Fig. 416.**—Individuality of the chromosomes in the eggs of *Ascaris* (BOVERI).

*E*, anaphase of the first cleavage; *F*, two-cell stage with lobed nuclei, the lobes formed by the ends of the chromosomes; *G*, early prophase of the ensuing division; chromosomes re-forming, centers dividing; *H*, later prophase, the chromosomes lying with their ends in the same position as before; centers divided.

**Figure 14: Images of cell division featuring the chromosomes and spindles. Wilson 1925**

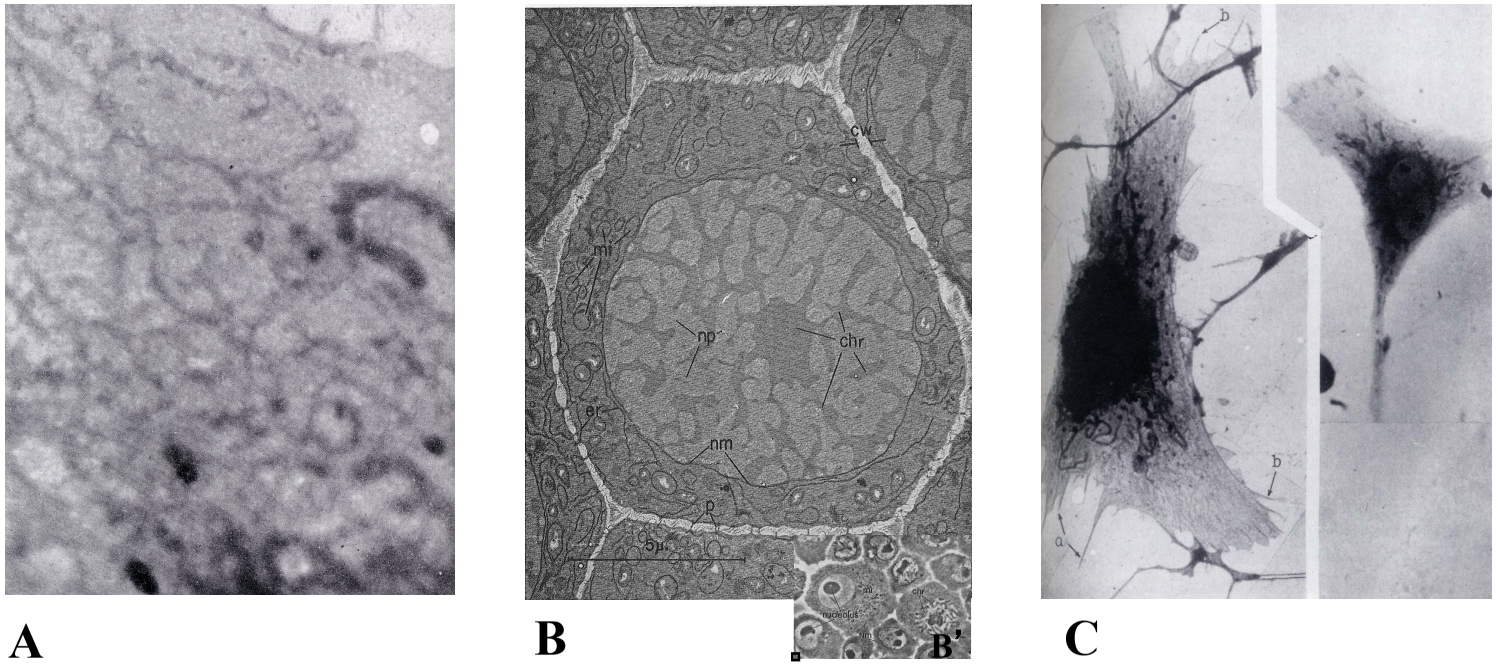
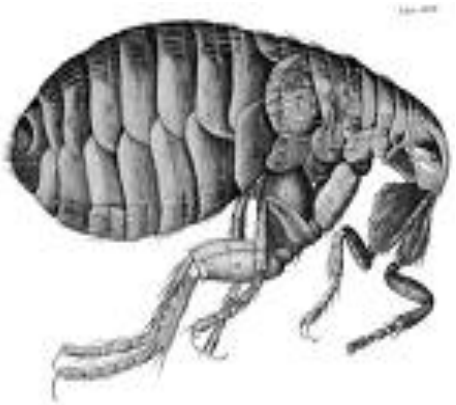
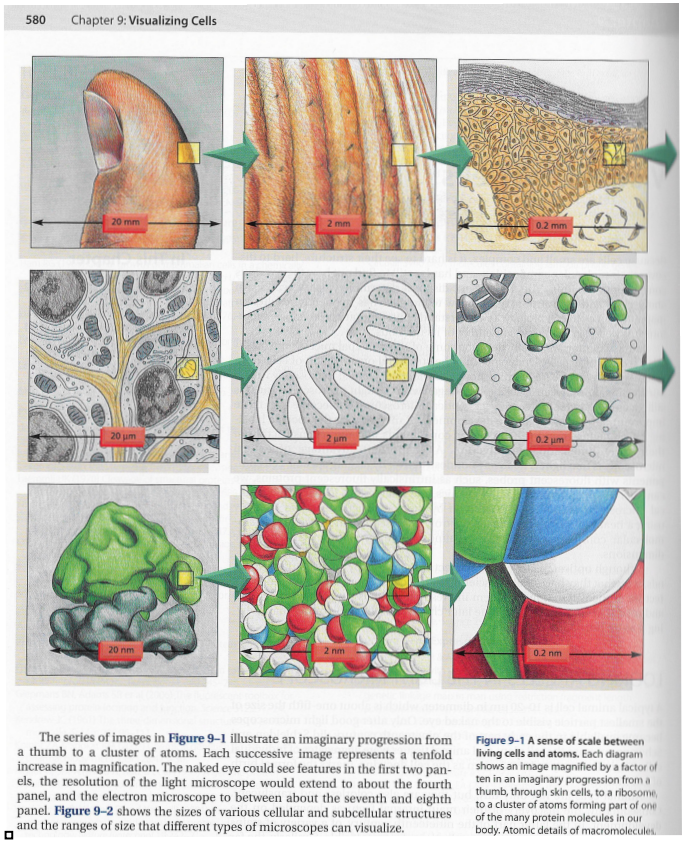



**Figure 15: Electron micrographs of cells. A) Porter, Claude and Fullam, 1945. B) De Robertis, 1965. B') De Robertis, 1965. C) Electron micrograph (left) and optical image (right) of a fibroblast, Porter, Claude and Fullam, 1945**

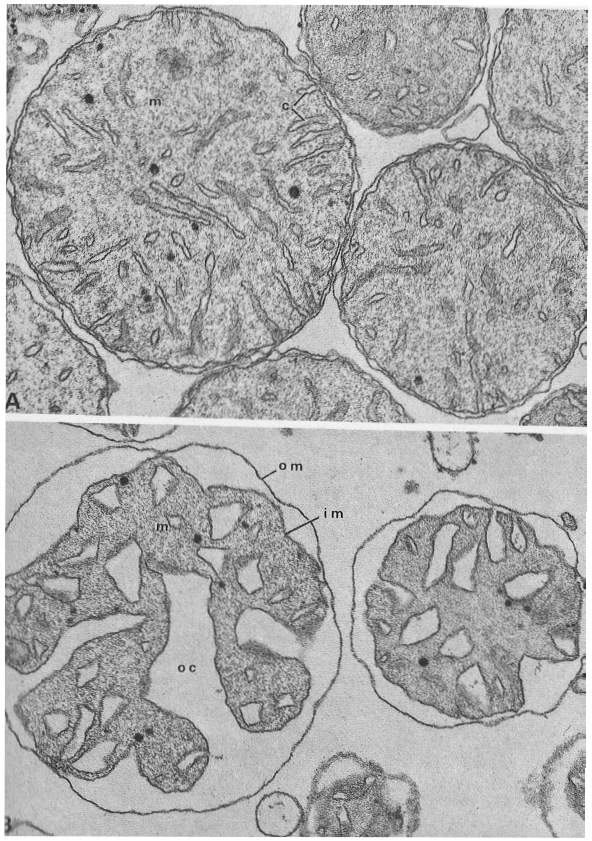


A

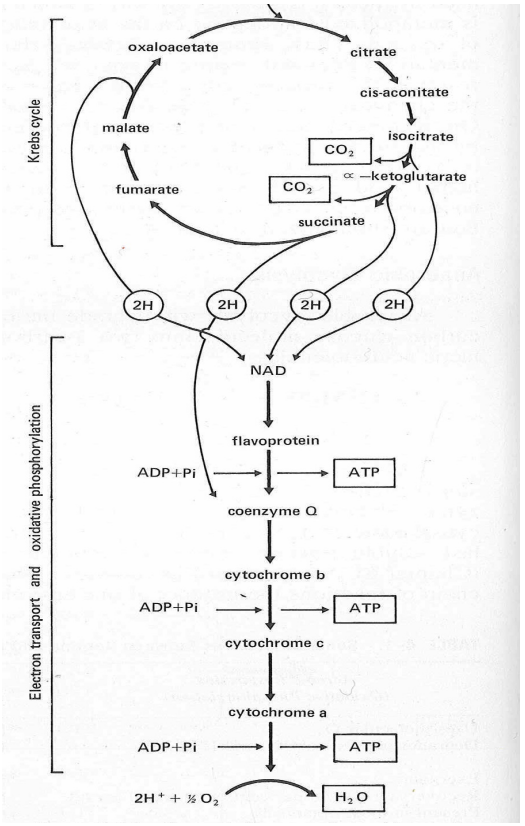



B

**Figure 16: Visual versions of the continuity of vision argument through time.**
**A) Hooke, 1666. B) Alberts et al, 2008**




A




B

**Figure 17: Electron micrograph image of mitochondria and molecular image image of Krebs cycle and oxydative phosphorylation. A) Electron micrograph image of mitochondria. De Robertis. 1987. B) Image of Krebs cycle and oxydative phosphorylation De Robertis, 1975**

**MOLECULAR CULTURE DEVELOPMENT IN ITS RELATION TO CELL BIOLOGY**

**VISUAL FORM**

**1st WAVE OF MOLECULARISATION (~1850-1930)** → **FIRST GENERATION MODELS**

* PAPER FORMULAE

**2nd WAVE OF MOLECULARISATION (~1930-1970)** → **SECOND GENERATION MODELS**

BIOCHEMICAL MODELS
* METABOLIC CYCLES (KREBS)

PHYSICOCHEMICAL MODELS
* 3D MODELS OF PROTEINS (COREY- PAULING)

MOLECULAR BIOLOGY MODELS
* DNA DOUBLE HELIX (WATSON/CRICK)
* DNA REPLICATION (MESELSON/STAHL)
* PROTEIN SYNTHESIS (CRICK/ORGEL)
* OPERON (JACOB/MONOD)

**3rd WAVE OF MOLECULARISATION (~1970-2000)** → **THIRD GENERATION MODELS**

* SIGNAL TRANSDUCTION/ INTERACTOMICS
* MEMBRANE EMBEDEED RECEPTORS WITH SIGNALLING FUNCTIONS
* ENDOPLASMIC RETICULUM PROTEIN SYNTHESIS AND PROCESSING

**Figure 18 A: The historical relation between molecular culture and cell biology (left) and its correspondent visual forms (right)**

**Figure 18 B: The different visual forms of molecular imagery:**
**a) Paper Formula (1st generation). b) Metabolic cycles (2nd generation). c) 3D models of proteins (2nd generation). d) DNA replication (2nd generation). e) Signal Transduction (3rd generation).**

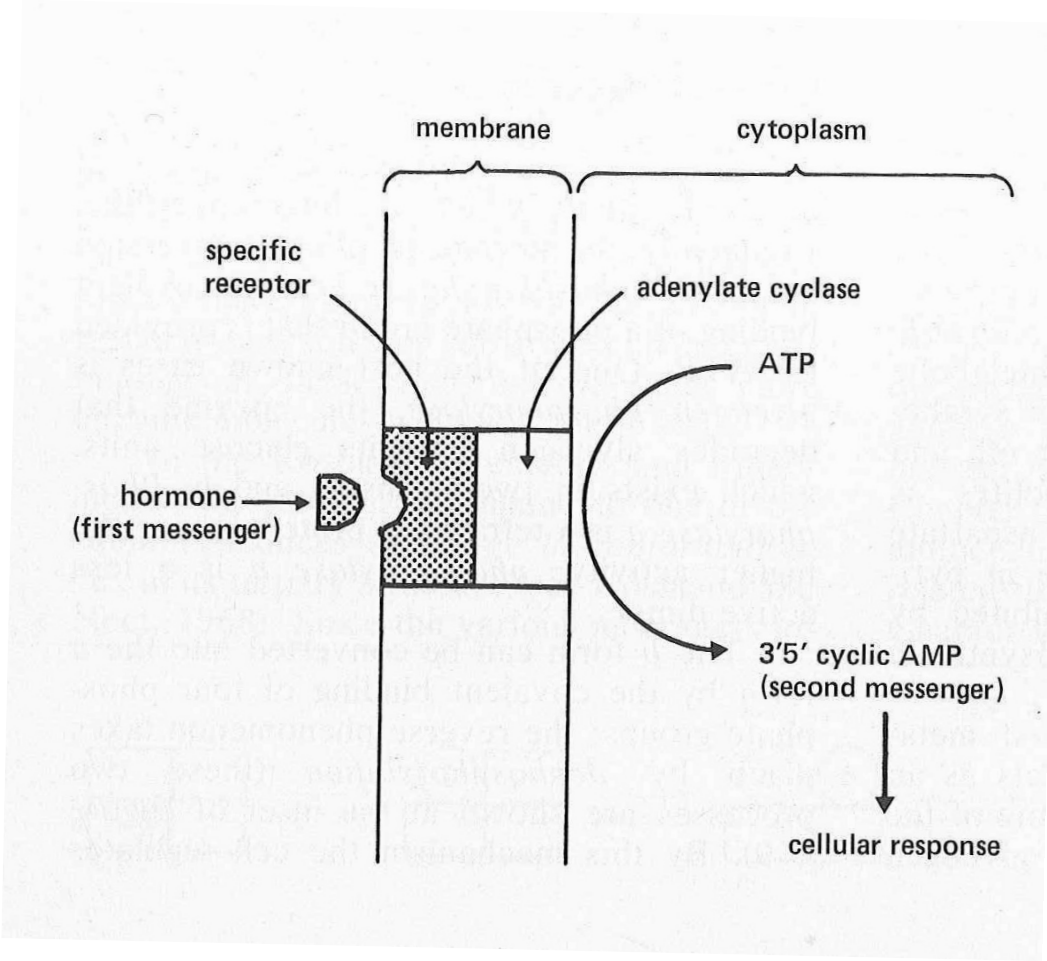
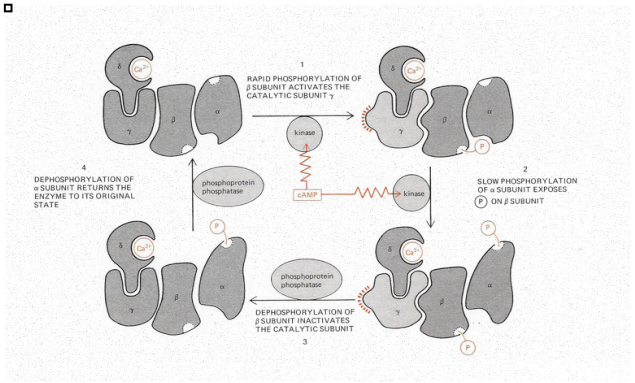
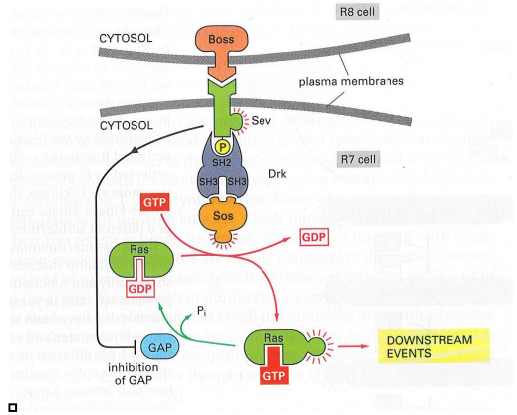


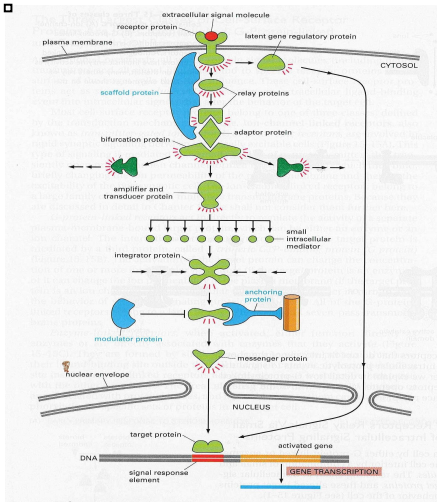

**Figure 19: The idea of signal transduction. De Robertis et al 1975**




1983




1994




2002

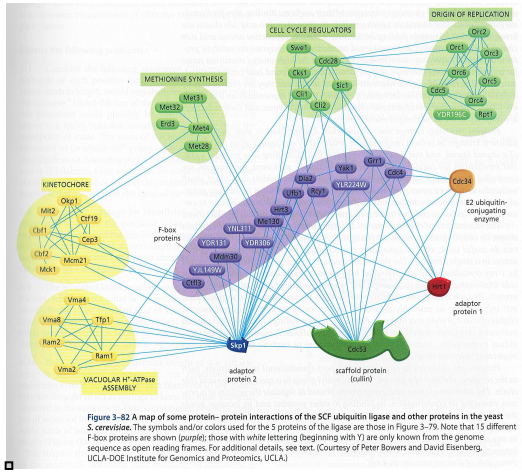



Figure 3–82 A map of some protein–protein interactions of the SCF ubiquitin ligase and other proteins in the yeast *S. cerevisiae*. The symbols and/or colors used for the 5 proteins of the ligase are those in Figure 3–79. Note that 15 different F-box proteins are shown (*purple*); those with *white* lettering (beginning with Y) are only known from the genome sequence as open reading frames. For additional details, see text. (Courtesy of Peter Bowers and David Eisenberg, UCLA-DOE Institute for Genomics and Proteomics, UCLA.)

2008

**Figure 20: The growth in complexity of signal transduction imagery through the successive editions of Alberts et al. MBC**

**Figure 21:** **Images of signal transduction pathways in biotech companies catalogs**

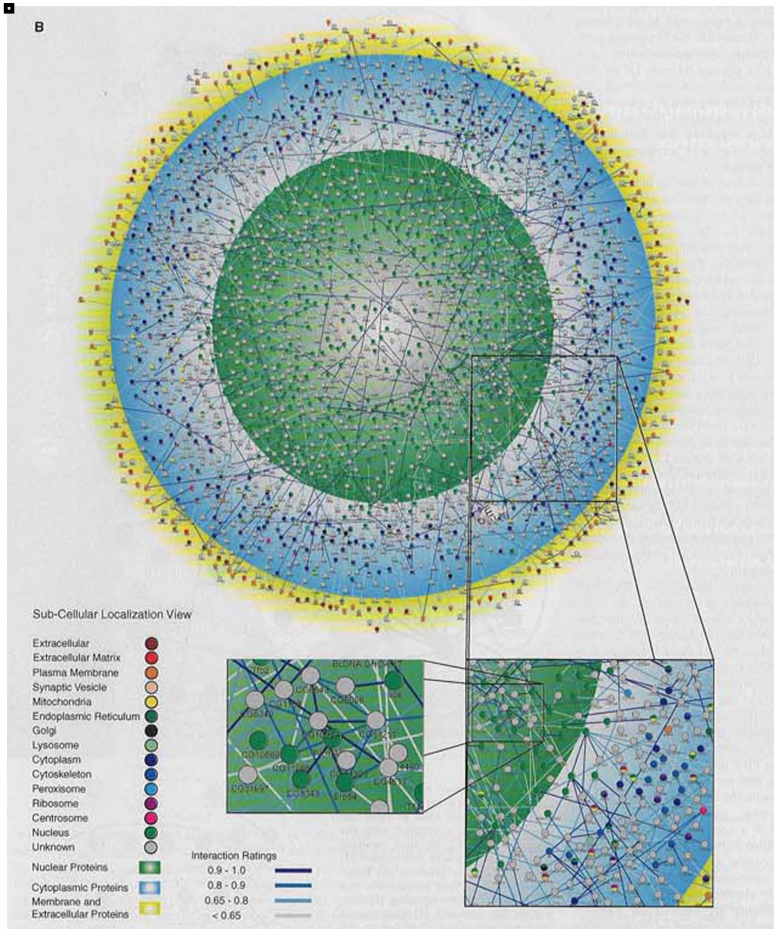



**Figure 22: The interactome. Giot. L, et al. Science 302. (2003)**

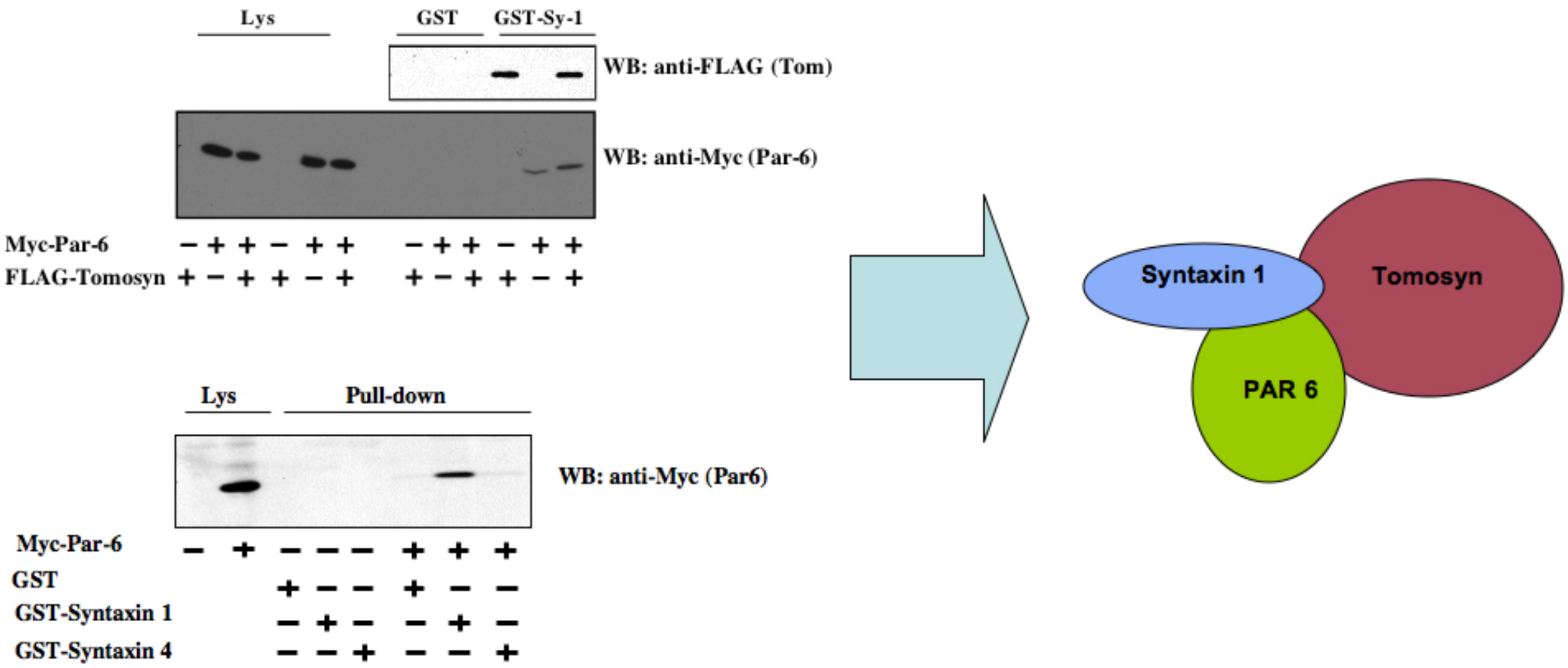



**Figure 23: Process of visual translation of molecular imagery of the 3rd order. Signal transduction imagery is constructed by the visual translation of the 'traces' left by molecules in an autoradiogram (left). Serpente, unpublished data**

## De Robertis et al Cell Biology

| Publication Years | 1948 | 1960 | 1965 | 1975 | 1980 | 1987 |
|---|---|---|---|---|---|---|
| Total numbers of pages | 345 | 555 | 446 | 615 | 647 | 734 |
| Total numbers of Images | 143 | 253 | 290 | 360 | 421 | 487 |
| Ratio (Images/Pages) | 0.41 | 0.45 | 0.65 | 0.58 | 0.65 | 0.66 |
| Average of Figures/ Chapter | 11.9 | 15 | 13 | 14 | 15 | 20 |

## Alberts et al Molecular Biology of the Cell

| Publication Years | 1983 | 1989 | 1994 | 2002 | 2008 |
|---|---|---|---|---|---|
| Total numbers pages | 1146 | 1218 | 1294 | 1463 | 1601 |
| Total numbers of Images | 1284 | 1463 | 1434 | 1713 | 1819 |
| Ratio (Images/Pages) | 1.12 | 1.20 | 1.11 | 1.17 | 1.14 |
| Average of Figures/ Chapter | 68 | 70 | 60 | 69 | 73 |

**Figure 24: The changing balance between images and text in cell biology textbooks 1940s-2000s**

**Figure 25: The MBC 'team' at Fort Hill, 1982. From left to right Bruce Alberts. Keith Roberts, Martin Raff,Kevin Borden, James Watson, Dennis Bray, Julian Lewis. (Picture courtesy of Keith Roberts)**

**Figure 26: Discussing the making of MBC at Fort Hill. 1982. From left to right: Martin Raff, James Watson, Bruce Alberts, Keith Roberts, Gavin Borden, Keith Porter, Miranda Robertson. (Picture courtesy of Keith Roberts)**

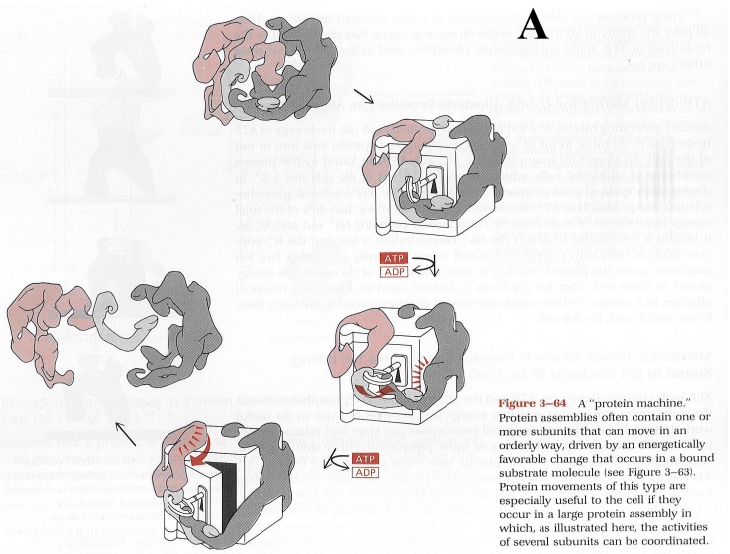



**Figure 3–64** A "protein machine." Protein assemblies often contain one or more subunits that can move in an orderly way, driven by an energetically favorable change that occurs in a bound substrate molecule (see Figure 3–63). Protein movements of this type are especially useful to the cell if they occur in a large protein assembly in which, as illustrated here, the activities of several subunits can be coordinated.

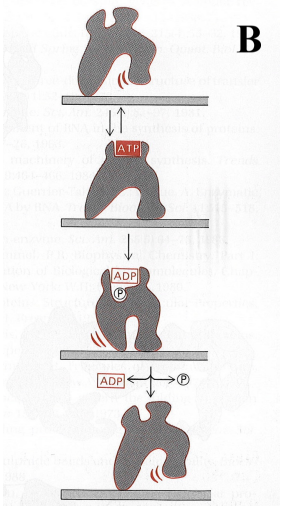



**Figure 3–63** An allosteric "walking" protein in which an orderly transition among three conformations is driven by the hydrolysis of a bound ATP molecule. Because one of these transitions is coupled to the hydrolysis of ATP, the cycle is essentially irreversible. By repeated cycles, the protein moves consistently to the right along the filament.

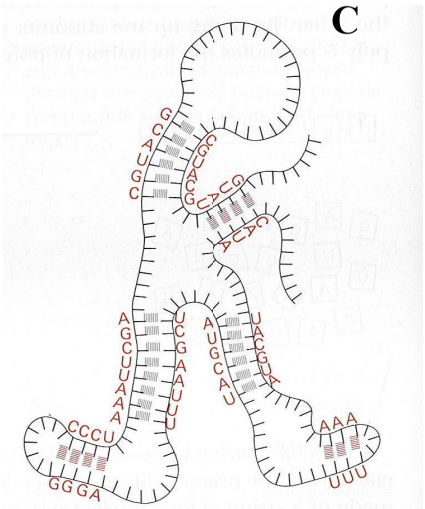



**Figure 1–6** Nucleotide pairing between different regions of the same polynucleotide (RNA) chain causes the molecule to adopt a distinctive shape.

**Figure 27: Anthropomorphic molecules. A) The 'safe cracker'. B) the 'walking tooth'. C) the 'human RNA'.**

**Alberts et al 1986**

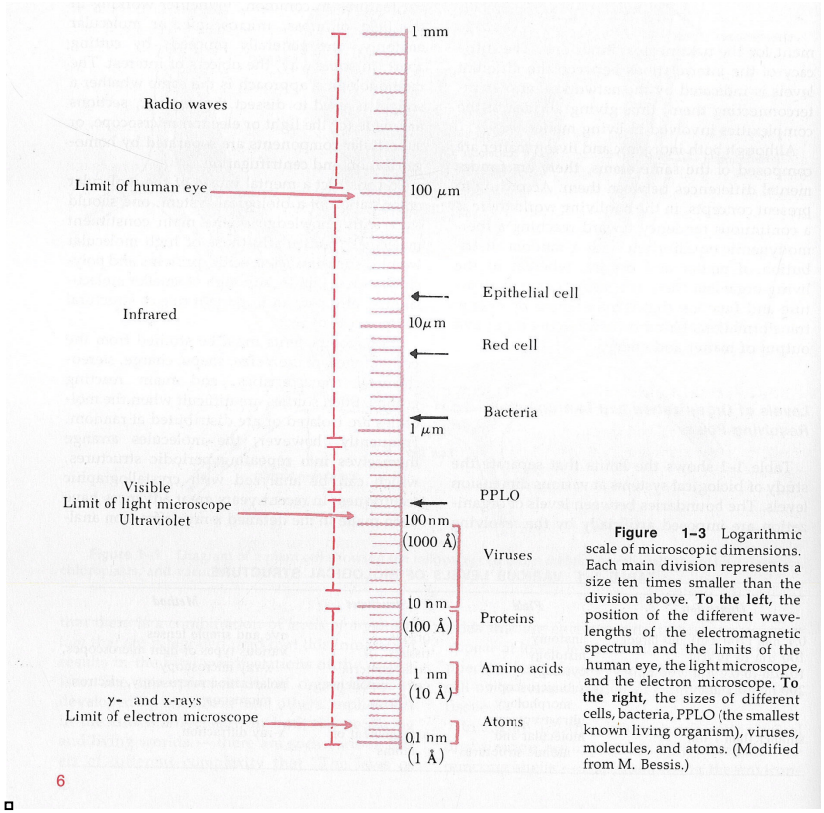



**Figure 1–3** Logarithmic scale of microscopic dimensions. Each main division represents a size ten times smaller than the division above. **To the left,** the position of the different wavelengths of the electromagnetic spectrum and the limits of the human eye, the light microscope, and the electron microscope. **To the right,** the sizes of different cells, bacteria, PPLO (the smallest known living organism), viruses, molecules, and atoms. (Modified from M. Bessis.)

**A**

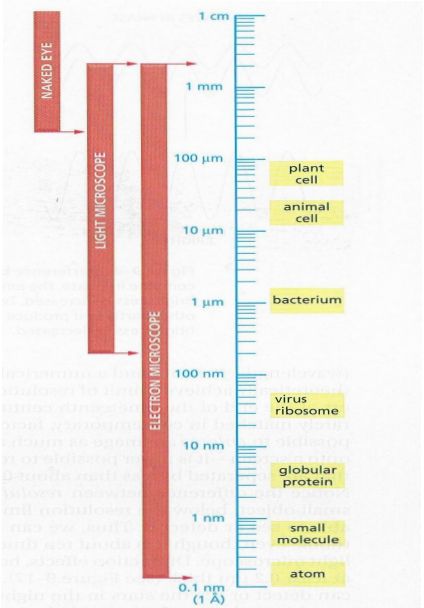



**Figure 9–2 Resolving power.** Sizes of cells and their components are drawn on a logarithmic scale, indicating the range of objects that can be readily resolved by the naked eye and in the light and electron microscopes. The following units of length are commonly employed in microscopy:
μm (micrometer) = $10^{-6}$ m
nm (nanometer) = $10^{-9}$ m
Å (Ångström unit) = $10^{-10}$ m

**B**

**Figure 28: The energy spectra in A) CB (1980) and B) MBC (2008)**

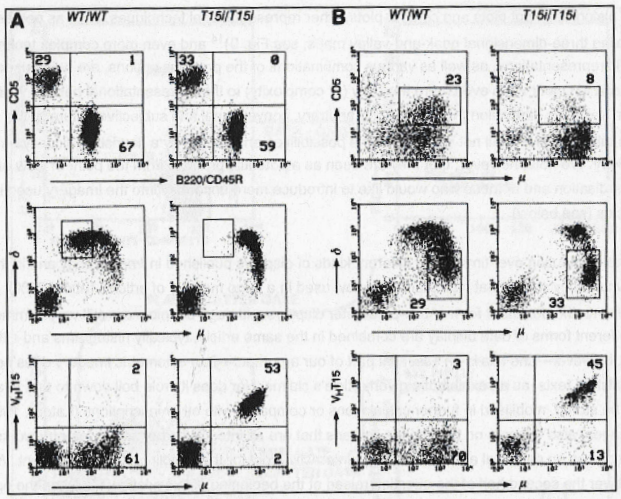



Fig. 3. Flow cytometric dot plots. The figure also illustrates the use of cursors and parallelograms to select (or 'gate') cell populations. Source: unpublished illustration kindly provided by Dr. Karl Rajewsky, Institute of Genetics, University of Köln (Germany).

A

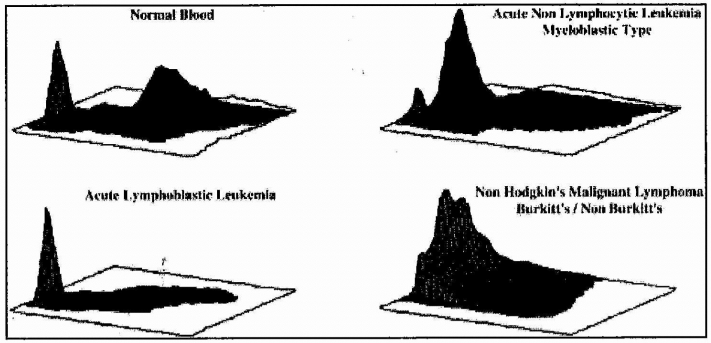



Fig. 9. Perspective plots as icons of normal and pathological conditions. Source: Immunopath advertisement, n.d.; original in colour. Reprinted by permission of Immunopath, Oncology and Immunology Laboratories, 7300 West 20th Avenue, Hialeah, Florida 33010, U.S.A.

B

**Figure 29: FACS dot plots and perspective plots of normal and pathological conditions. (A and B respectively) From Cambrosio and Keating 2000**

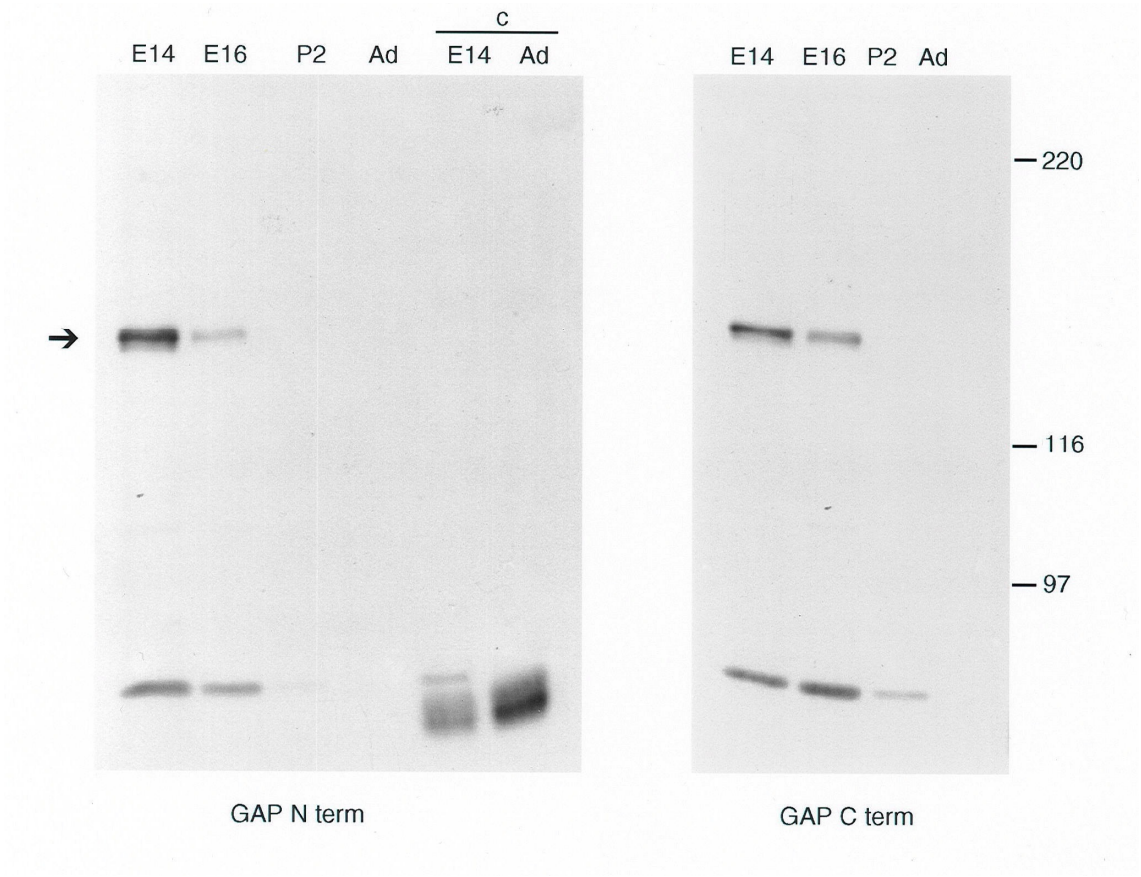



**Figure 30: Autoradiogram from an Immunoprecipitation/Western blotting experiment. Serpente et al. 1996**

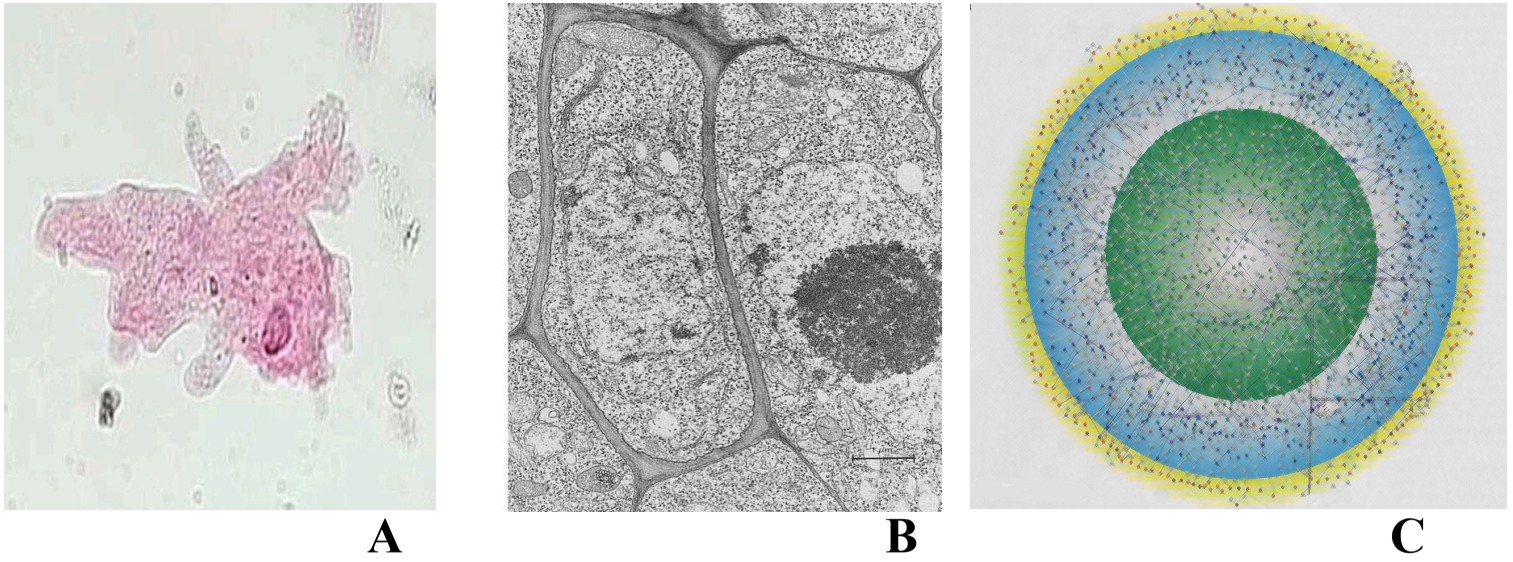



**Figure 31: Images of cells: A)** ***Amoeba*** **as seen through a light microscope x 100. B) Electron Micrograph of a transverse section of a root tip of the bean Phaseolus Vulgaris. Source: de Duve (1984). C) A protein-protein interaction map 'interactome' Giot L,** ***et al.*** **Science (2003)**

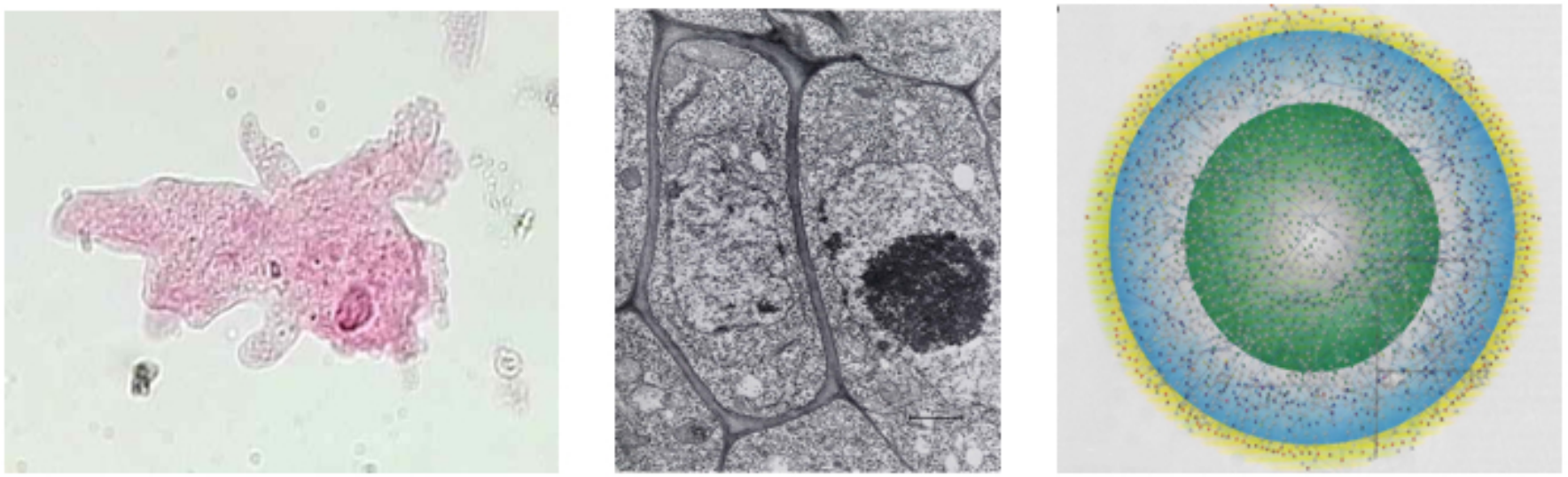



**Figure 32: Images of cells through the semiotic lens**

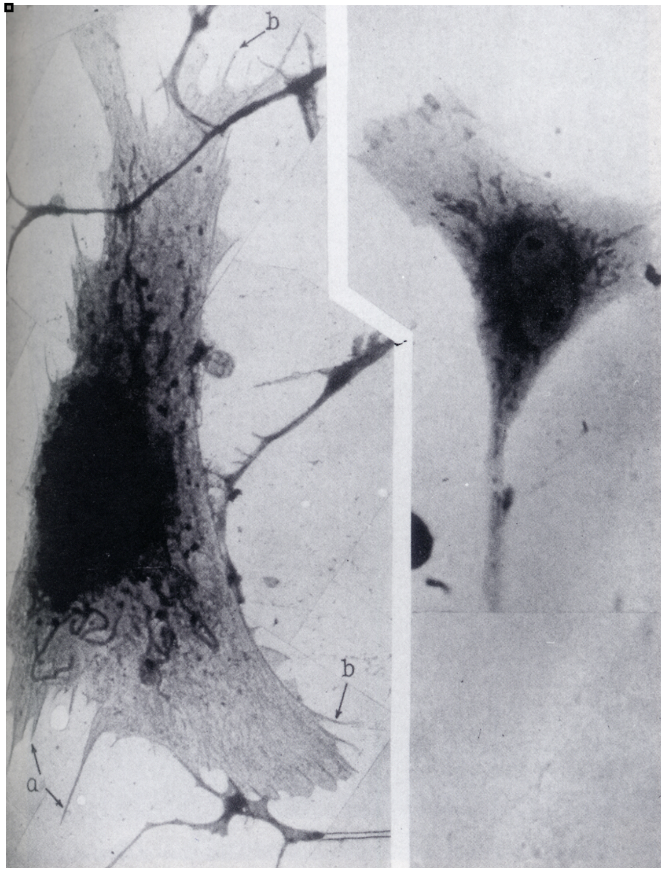



**Figure 33: The construction of indexicality.**
**Electron micrograph (left) and optical image of a cultured fibroblast**
**Porter, Claude and Fullam, 1945**

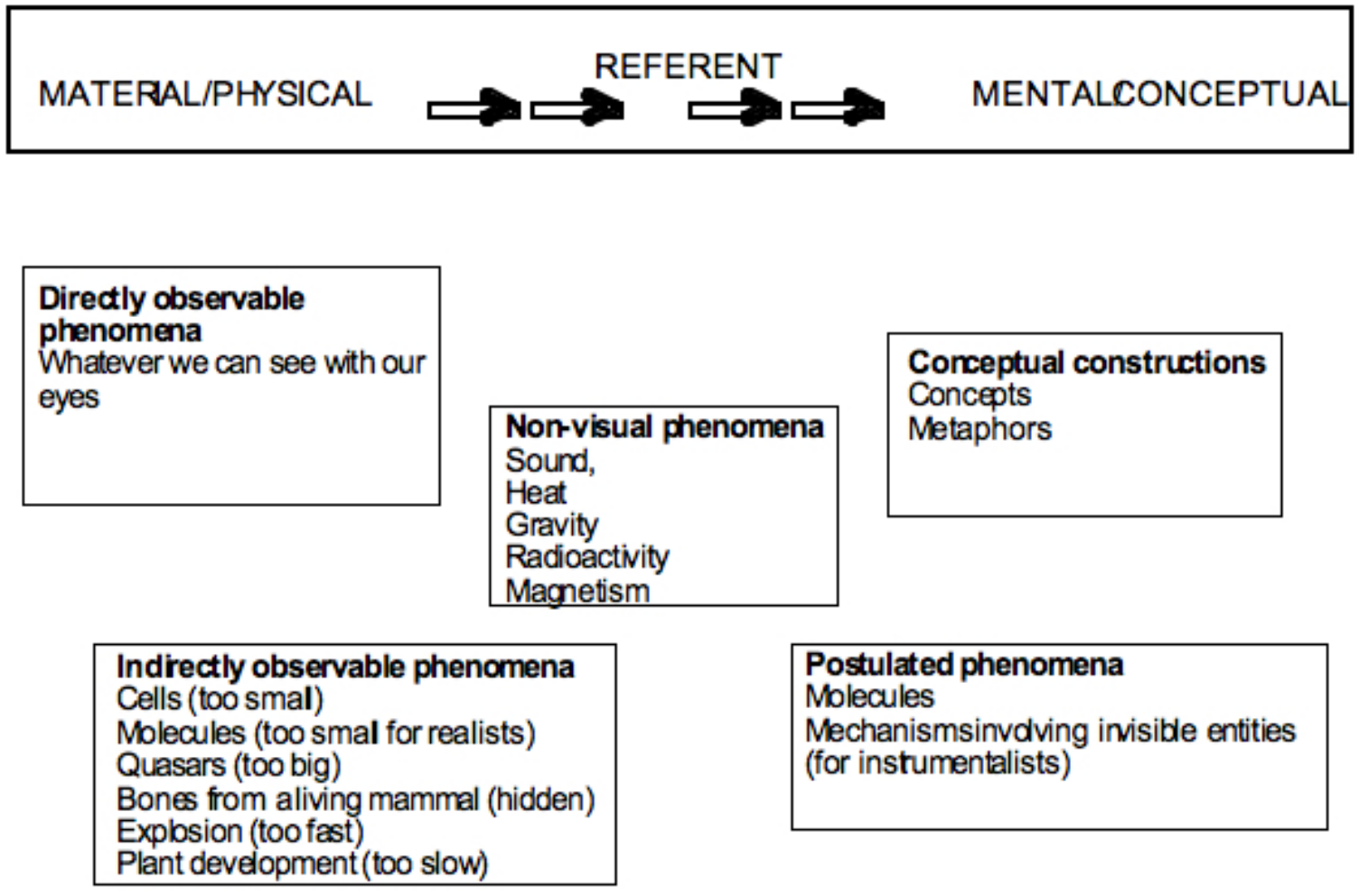



**Figure 34: The distinctive nature of the Referent. Adapted from Pauwels 2006**

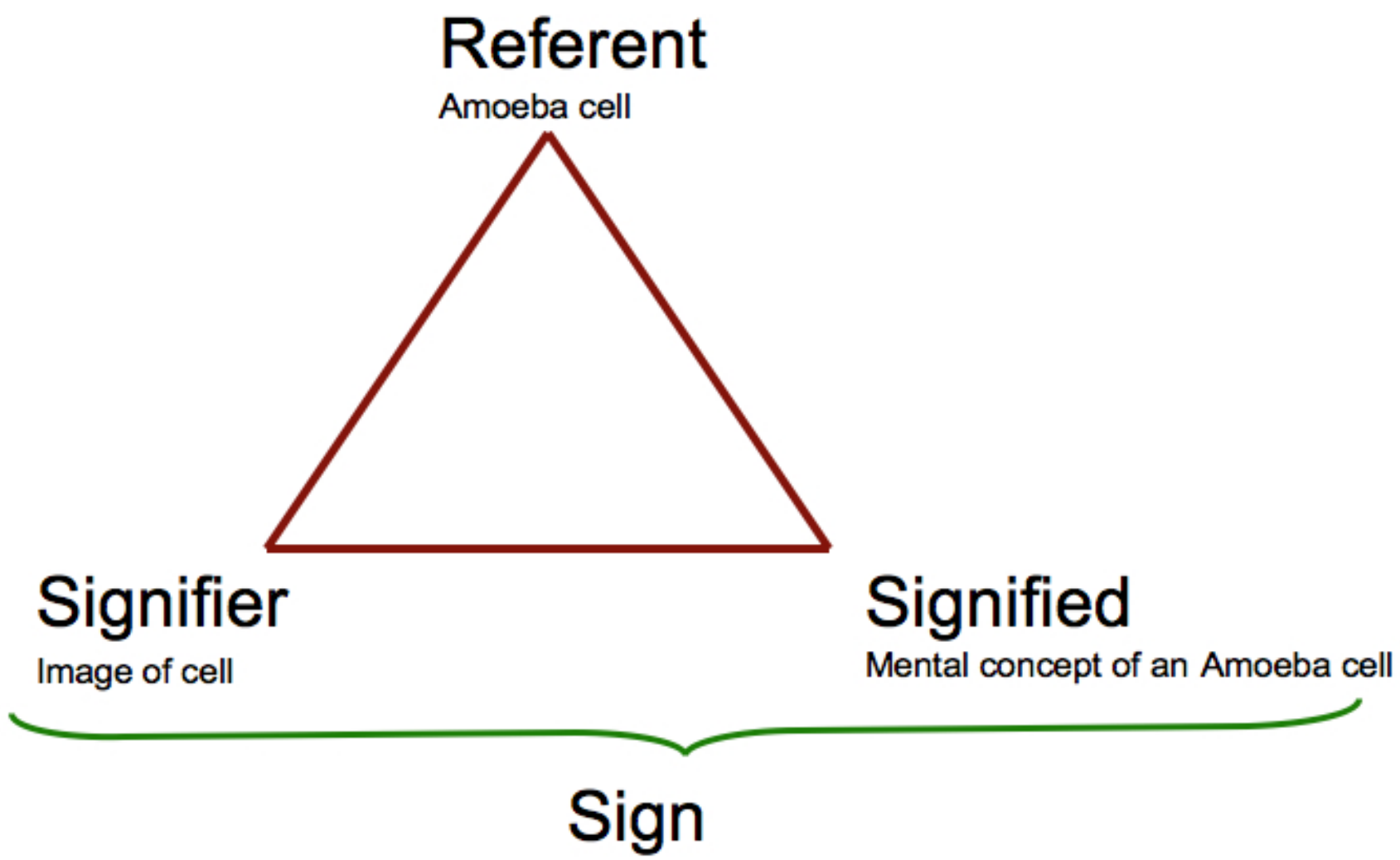



**Figure 35: The triangle of signification**

**Right Depiction**

---

**Representation**

Based on the idea of fidelity to nature

**Presentation**

Based on the idea of mixing
the artifactual and the natural
and the simultaneity of seeing
and making.

---

**Truth to Nature** | **Mechanical Objectivity** | **Trained Judgement** | **Hybrid Practices**

Mid 17th cent. ----------

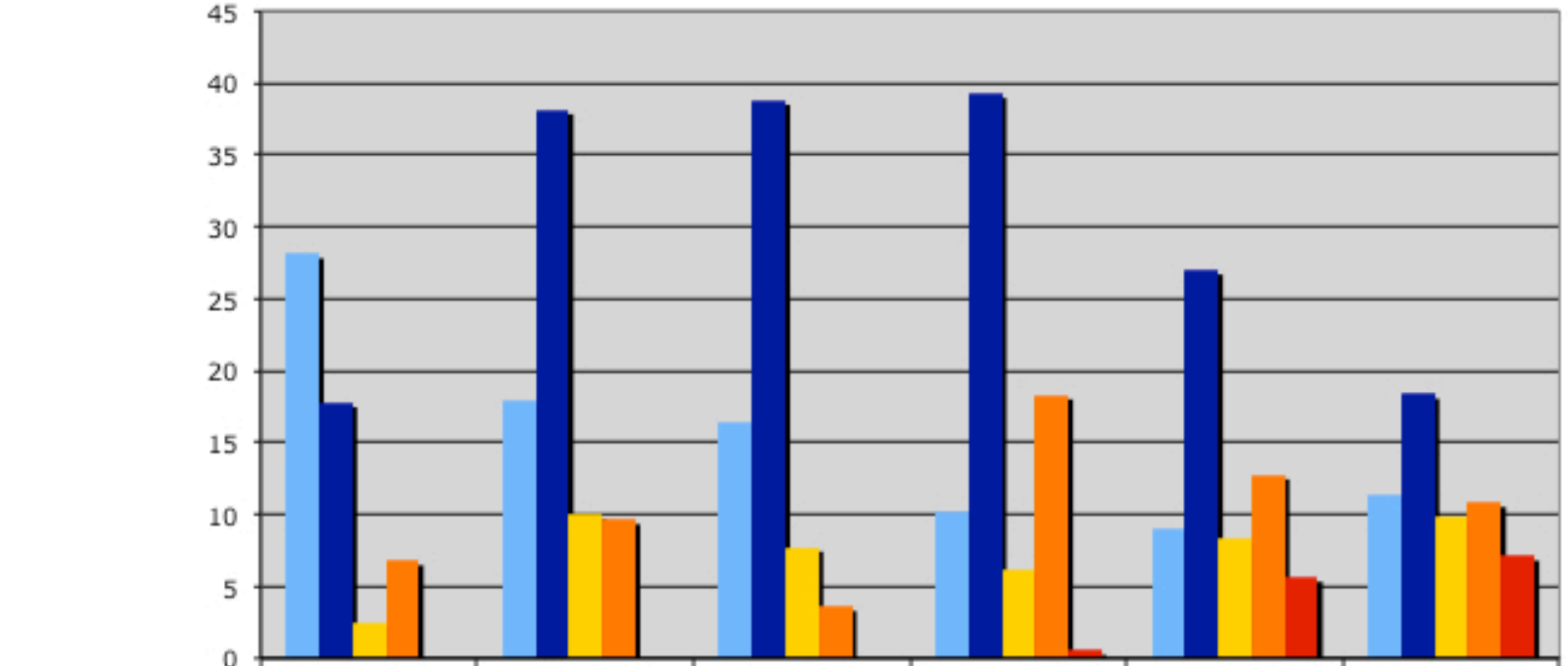
Mid 19th cent.----------

Mid 20th cent. ----------

Late 20th cent.----------

**Figure 36: The historical dimension of 'Objectivity'. Adapted from Daston and Galison 2007**

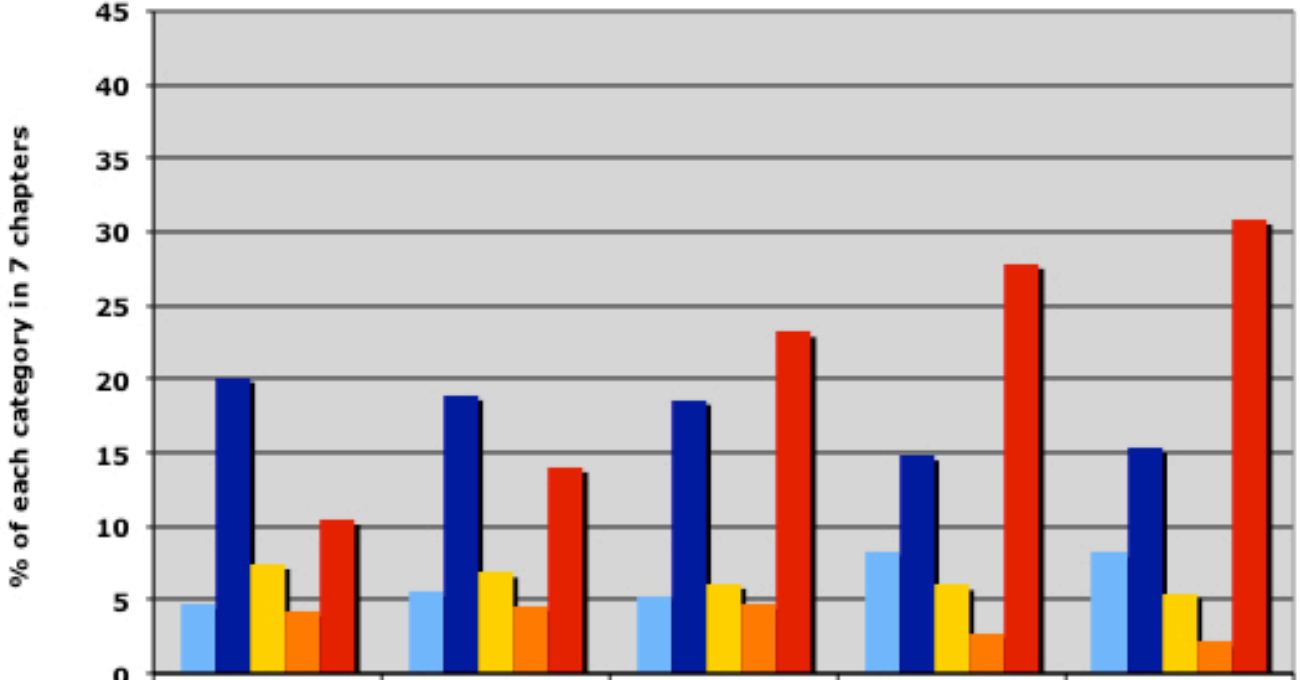
## GRAPH 1 De Robertis et al




| | 1948 | 1960 | 1965 | 1975 | 1980 | 1987 |
|---|---|---|---|---|---|---|
| light microscope | 28.15 | 17.9 | 16.48 | 10.16 | 9.02 | 11.42 |
| e-microscope | 17.8 | 38.17 | 38.82 | 39.3 | 27.02 | 18.39 |
| cellular models | 2.52 | 9.99 | 7.75 | 6.2 | 8.42 | 9.78 |
| e- based models | 6.81 | 9.67 | 3.63 | 18.34 | 12.78 | 10.86 |
| Molec. 3rd gen | 0 | 0 | 0 | 0.57 | 5.66 | 7.13 |

**Publications Years**

## GRAPH 2 Alberts et al




| | 1983 | 1989 | 1994 | 2002 | 2008 |
|---|---|---|---|---|---|
| light microscope | 4.68 | 5.5 | 5.29 | 8.3 | 8.22 |
| e- microscope | 20.12 | 18.9 | 18.6 | 14.81 | 15.34 |
| cellular models | 7.42 | 6.86 | 6.09 | 6 | 5.47 |
| e- based models | 4.23 | 4.57 | 4.69 | 2.75 | 2.12 |
| Molec. 3rd gen | 10.45 | 14.01 | 23.2 | 27.84 | 30.85 |

Publications Years

## APPENDIX

### A.1. Primary sources.

Two textbooks were selected to perform this analysis. The first textbook is *Molecular Biology of the Cell* (MBC), which was first published in 1983 by Bruce Alberts, Dennis Bray, Julian Lewis, Martin Raff, Keith Roberts and James Dewey Watson. MBC has a total of five editions up to present. The second (1989) and third (1994) editions, with the same set of authors, and a fourth (2002) and fifth (2008) authored by Bruce Alberts, Alexander Johnson, Julian Lewis, Martin Raff, Keith Roberts and Peter Walter. The second textbook selected is *General Cytology*, first published in English in 1948 (original in Spanish, 1946) by Eduardo P D De Robertis, Francisco Saez and Wiktor Nowiski. *General Cytology* has a total of eight editions, the second (1954), the third (1960) and the fourth (1965) with the same set of authors. The fifth edition (1970) has the same authors, but it changed its title to *Cell Biology* (CB). The sixth edition (1975) kept the same title but was authored by Eduardo D P De Robertis, Francisco A Saez and Edward M De Robertis (Eddie De Robertis). The seventh (1980) and eight (1987) editions were published under the name of *Cell and Molecular Biology* and were co-authored by Eduardo D P De Robertis & Eddie De Robertis.[844] Whereas my analysis include all the editions of MBC, only six out of the eight editions published (1948, 1960, 1965, 1975, 1980 and 1987) of CB were surveyed, since those of 1954 and 1970 were not available. Important general information such as the number of pages, and images, their ratio, etc for the different editions of De Robertis et al and Alberts el al could be found in **Figure 24,** (see page 109).

### A.2. Quantitative analysis of textbooks.

The first step consisted in constructing one table for every assessed edition of either CB or MBC. Tables 1, 2, 3 4, 5 and 6 for the 1948, 1960, 1965, 1975, 1980 and 1987 editions respectively of CB, and tables 7, 8, 9, 10 and 11 for the 1983, 1989, 1994,

844 To avoid confusion do to the diversity of titles and changing authorship in the textbooks assessed, I use indistinctively on the one hand ‘MBC’ or ‘Alberts et al’ and ‘CB’ or ‘De Robertis et al’ on the other to generically refer to each textbook, following for the year of publication of each edition when required.

2002 and 2008 editions respectively of MBC. Each table contains the total number of images for each of the 7 categories defined previously in chapter 1. Briefly here, these categories are 1) Optical images obtained with different types of light microscopes. 2) Images obtained with an electron microscope. 3) Images of drawings of cells or cells components, not involved in any kind of cellular mechanism. 4) Images of cellular models with no reference to specific molecules. 5) Images of models based on images taken with an electronic microscope, ($e^-$ based models). 6) Images of molecular models of the third-generation. 7) All other pictorial forms, such as diagrams, charts, pictures or drawings of instruments and or techniques, DNA or protein electrophoresis gels, autoradiograms, apparatuses, and the depiction of molecules in their own without any involvement in any type of cellular processes.

The total number of images for each category was selected from seven different chapters from each edition of either CB or MBC. The selection of the chapters was based on the following criteria. A) Similarity of subjects/themes, such as 'cell membrane', 'mitochondria and energy production', or 'the cytoskeleton and cell mobility', in the content of chapters in the different editions of both textbooks. The idea was to facilitate the comparison process between both textbooks throughout the years. Seven was the minimum number of chapters that allowed for this comparison. The inclusion of an extra chapter would have meant the inclusion of a subject without an equivalent comparable one in the others editions and/or textbooks. B) Selection of chapters on cellular themes rather than molecular ones. The selection of chapters explaining cellular processes as performed by cells themselves (movement, secretion, morphogenesis, etc) is central for this work, for it allows us to investigate the growth of the molecular visuality and molecular explanation inside cell biology since the time the third wave of molecularisation entered cell biology in the 1980s to the present. Moreover, chapters on cellular themes show more continuity in the different editions of both CB and MBC. Chapters devoted exclusively to molecular themes such as DNA replication, protein synthesis or gene regulation, were excluded to avoid biases towards the other visual forms of molecular imagery (second wave) on the quantitative analysis (also because they are non- existent in the editions of 1948 and 1960 of CB). In relation to this, all molecular imagery belonging to the first and second wave of molecularisation such as metabolic

cycles, protein synthesis excluding protein maturation processes and/or post-translational processes such as glycosilation and no associated to endoplasmic reticulum was grouped in category 7, 'all other pictorial forms', (see chapter 1). Also part of this category (7) were figures of a hybrid nature and/or resilient nature for classifying in any of the categories mentioned.

The total number of images from all categories for each of the seven chosen chapters was considered to be 100% and taken as the basis to calculate the percentage of each category (1-7) for each chapter. The percentages per category were added and then divided by the total amount of chapters (7). The resultant value corresponds to the percentage average of that category for that corresponding edition. The averages values from categories 1-2-4-5-6 (see chapter 1) were used to construct the graphs for all the editions of each textbook (**Graph 1** for De Robertis et al and **Graph 2** for Alberts et al, see pages 114 and 117 respectively). In them the four categories chosen for their centrality of the analysis (1-2-4-5-6) were relabeled respectively as follows: (1) Images obtained with a light microscope, (Light microscope, light blue bar), (2) Images obtained with an electron microscope (e- microscope, dark blue bar), (4) Images of cellular models (yellow bar), (5) Images created from electron micrographs (e- based models, orange bar), and (6) Third-generation of models of molecular nature (red bar).

### A.3. Sources of Figures.[845]

**Figure 1: The Visual Change in Cell Biology: From the microscopic to the molecular image.** Left panel: Image of a mouse embryonic fibroblast taken with an optical microscope from:
http://www.biomedcentral.com/bmccellbiol/imageofthemonth/archive/2009/01
(consulted april 2011) Right panel: 'Global views of the protein-interaction map'. Science, 2003, 302: 1733, 2003. Fig 4.

**Figure 2: The different types of images found in cell biology textbooks**
Upper row, first image on the left. Photomicrograph in phase contrast of the living cells from an ascitic tumor. De Robertis, et al. 1965. Fig 2-2, pp. 14.

845 For each figure the original title given in the dissertation is provided (in bold) followed by the original title on the source alongside the source from which it belongs, its original figure number and the page were is located. For figures made especially for this dissertation, the title is given followed by the words 'authors figure'.

Upper row, second image from the left. Diagram of the Krebs or tricarboxylic acid cycle in mitochondria. De Robertis, et al. 1987. Fig 11-11, pp. 307.
Upper row, third image from the left. Hypothetical model of a red cell membrane showing the lipid bylayer. De Robertis, et al. 1980. Fig 8-4, pp. 137.
Up row, fourth image from the left. Tetrameric model of a cholinergic receptor. De Robertis, et al. 1975. Fig 24-25, pp. 568.
Middle row, first image from the left. Structure of an ameba. De Robertis, et al. 1965. Fig 21-1, pp. 380.
Middle row, second image from the left. One way in which signalling through PI-3 kinase promotes cell survival. Alberts, et al. 2002. Fig 15-60, pp. 882.
Middle row, third image from the left. A, electron micrograph of the smallest lamellar structure found in lipid-protein-water preparations. B, diagram showing the probable arrangement of lipid and protein molecules in such a membrane. De Robertis, et al. 1965. Fig 7-7, pp. 107
Bottom row, first image from the left. Curve representing the effect of deoxycholate on liver microsomes. De Robertis, et al. 1965. Fig 10-16, pp. 159.
Bottom row, second image from the left. Analysis of protein samples by SDS PAGE. Alberts, et al. 2002. Fig 8-15, pp. 486.
Bottom row, third image from the left. A membrane phospholipid molecule has a hydrophilic head and two hydrophobic tails. De Robertis, et al. 1980. Fig 5-9, pp. 81.
Bottom row, fourth image from the left. Electron micrograph of a root-tip cell stained with osmium and other heavy metal ions. Alberts, et al. 1994. Fig 4-20, pp. 151.
Bottom row, fifth image from the left. Two distintic early endosomal compartments in an epithelial cell. Alberts, et al. 1994.
Fig 13-35, pp. 626.

**Figure 3: Images of cells or cells components taken with an optical microscope**
A) Photomicrograph in phase contrast of the living cells from an ascitic tumor. De Robertis, et al. 1965. Fig 2-2, pp. 14. B) The course of mitosis in a typical animal cell. (early prophase). Alberts, et al. 2002. Fig 18-8, pp. 1033.

**Figure 4: Images of cells or cells components taken with an electronic microscope.**
A) Electron micrograph of a promeristematic cell of the root of *Allium sativum*. De Robertis, et al. 1965. Fig 2-4, pp. 16. B) Electron micrograph of a root-tip cell stained with osmium and other heavy metal ions. Alberts, et al. 1994. Fig 4-20, pp. 151.

**Figure 5: Drawings of cells or cells components (isolated chromosomes, membranes, mitochondria. etc.)**
A) Structure of an ameba. De Robertis, et al. 1965. Fig 21-1, pp. 380.
B) An aberrant human chromosome. Alberts, et al. 2008. Fig. 4-12, pp. 204.

**Figure 6: Images of cellular models**
A) Diagrammatic interpretation of the mechanism of secretion in the chromaffin cell. De Robertis, et al. 1980. Fig 11-13, pp. 243. B) Two distintic early endosomal compartments in an epithelial cell. Alberts, et al. 1994. Fig 13-35, pp. 626.

**Figure 7: Models based on images obtained with an electronic microscope.**

A) A, electron micrograph of the smallest lamellar structure found in lipid-protein-water preparations. B, diagram showing the probable arrangement of lipid and protein molecules in such a membrane. De Robertis, et al. 1965. Fig 7-7, pp. 107.
B) The myosin-II thick filament.
A, electron micrograph of a myosin-II thick filament isolated from frog muscle. B, schematic diagram, not drawn to scale. Alberts, et al. 1994. Fig 16-88, pp. 851.

**Figure 8: Molecular models belonging to the molecular culture (3rd generation models second order).**
A) A hypothetical model for the insertion of an internal loop of polypeptide chain into the lipid bilayer of the ER. Alberts, et al. 1986. Fig 8-46, pp. 443. B) One way in which signalling through PI-3 kinase promotes cell survival. Alberts, et al. 2002. Fig 15-60, pp. 882.

**Figure 9: All other pictorial forms: A) molecules (1st and 2nd generation models molecular culture, B) diagrams, charts. C) gels, apparatuses etc.**
A) A membrane phospholipid molecule has a hydrophilic head and two hydrophobic tails. De Robertis, et al. 1980. Fig 5-9, pp. 81.
B) Curve representing the effect of deoxycholate on liver microsomes. De Robertis et al, 1965. Fig 10-16, pp. 159. C) Polyacrylamide gel showing he sequence of bacteriophage ϕ x 174. De Robertis, et al. 1980. Fig 21-8, pp. 476.

**Figure 10: Schann's drawings of different cell types.**
Plates illustrating Teodor's Schwann Mikroskopiche Unntersuchungen. From de Duve, 1984, Chapter 1, pp 8.

**Figure 11: The Ideal Cell type.**
A) General diagram of a cell. Wilson, 1925. Fig 6, pp. 23. B) Diagram of a typical cell based on electron micrographs available in 1960. Brachet, et al. 1961. Fig 1.1, pp. 17. C) Map of the cell. De Duve, 1984.Chapter 1, pp 19.

**Figure 12: The contrasting imagery of the cytoplasm (left) and the cell nucleus (right)**
Left Panel. *Amaeba Proteus.* Wilson, 1925. Fig 3, pp 7. Right Panel. A small portion of the epidermis of a larval salamander. Wilson, 1925. Fig 1, pp 3.

**Figure 13: 1920s images of the cytoplasm.**
a, protoplasm of the egg of the sea-urchin. b, protoplasm from a living starfish egg.
c, the same in dying conditions. d, protoplasm from a young ovarian egg. Wilson, 1925. Fig 28, pp. 73.

**Figure 14: Images of cell division featuring the chromosomes and spindles.**
Left Panel. The later stages of mitosis in the egg of sea-urchin, *Toxopneustes*. Wilson, 1925. Fig 58, pp. 135. Right panel. Individuality of the chromosomes in the eggs *Ascaris*. Wilson, 1925.
Fig 416, pp 891.

**Figure 15: Electron micrographs of cells.**

A)Electron micrograph of small section of cultured chick fibroblast Thinner portion of cell […] shows a granular background and details of a darker lace-like reticulum which in places appear to be made of chains of vesicles. Porter, Claude and Fullam, 1945. Plate 14, Figure 16. B) Electron micrograph of a promeristematic cell of the root of *Allium sativum*. De Robertis, et al. 1965. Fig 2-4, pp. 16. C) Electron microscopy of cultured cells. (Chicken fibroblast cells grown on plastic film in tissue culture; left image by electron microscope; right imaged by light microscope. Porter Claude and Fullam, 1945, 81: 233-55, plate 10, in p. 247.

**Figure 16: Visual versions of the continuity of vision argument through time.**
A) Hooke, 1666. Left , Schem XXI, right (fly). Right, Schem XXXIV (flea)
B) A sense of scale between living cells and atoms. Alberts, et al. 2008. Fig 9-1, pp. 580.

**Figure 17: Electron micrograph image of mitochondria and molecular image image of Krebs cycle and oxydative phosphorylation.**
A) Electron micrographs of isolated mitochondria from rat liver in two extreme conformation states. De Robertis, et al. 1987. Fig 11-17, pp. 317. B) General diagram of aerobics respiration showing the Krebs cycle, the respiratory chain and its coupling with oxidative phosphorylation. De Robertis, et al. 1980. Fig 6-13, pp. 111.

**Figure 18 A: The historical relation between molecular culture and cell biology (left) and its correspondent visual forms (right)**

**Figure 18 B: The different visual forms of molecular imagery:**

**Figure 19: The idea of signal transduction.**
Diagram showing the effect of a hormone (first messenger) upon a specific receptor of a cell membrane and its effects on the enzyme adenylate cyclase. De Robertis, et al. 1975. Figure 4-8, pp. 66.

**Figure 20: The growth in complexity of signal transduction imagery through the successive editions of Alberts et al. MBC**
Top left: One proposed mechanism to explain the switch like activation and inactivation of phosphorylase kinase following a rise in intracellular cyclic AMP concentration. Alberts et al 1983. Figure 13-32, pp. 747.): Top right: Early cell signalling events in R7 development. Alberts et al 1994. Figure 15-53, pp. 765. Bottom left: Different kinds of intracellular signalling proteins along along a signalling pathway from a cell-surface receptor to the nucleus. Alberts et al 2002, Figure 15-16, pp 844. Bottom right: A map of some protein-protein interactions of the SCF ubiquitin ligase and other proteins in the yeast S.cerevisiae. Alberts, et al. 2008. Figure 3-82, pp. 189.

**Figure 21: Images of signal transduction pathways in biotech companies catalogs**

**Figure 22: The interactome.**
Global views of the protein-interaction map. Giot, et al. Fig 4. *Science* vol 302: 1733, 2003.

**Figure 23: Process of visual translation of molecular imagery of the 3rd order.**

Serpente, unpublished data (2004).

**Figure 24: The changing balance between images and text in cell biology textbooks 1940s-2000s.**

**Figure 25: The MBC 'team' at Fort Hill, 1982.** Courtesy of Keith Roberts (2007).

**Figure 26: Discussing the making of MBC at Fort Hill. 1982.** Courtesy of Keith Roberts (2007).

**Figure 27: Anthropomorphic molecules.**
A) A protein machine, Alberts, et al. 1986, Figure 3-64, pp. 132. B) An allosteric walking protein, Alberts et al, 1986, Figure 3-63, pp.131. C) Nucleotide pairing between different regions of the same polynucleotide (RNA). Figure 1-6, pp.6.

**Figure 28: The energy spectra.**
A) Logarithmic scale of microscopic dimensions, De Robertis, et al. 1980 Fig 1-3, pp. 6. B) Resolving power. Alberts, et al. 2008, Figure 9-2, pp. 581.

**Figure 29: FACS dot plots and perspective plots of normal and pathological conditions.**
Cambrosio, et al. 2000, A) Flow cytometric dot plots. Fig 3, pp. 241. B) Perspective plots as icons of normal and pathological conditions, Fig 9, pp. 263.

**Figure 30: Autoradiogram from an Immunoprecipitation/Western blotting experiment.**
Association of GAP with FAK during cortical development. Serpente, et al. 1996, Fig. 8, pp. 399.

**Figure 31: Images of cells.**
Images of cells: A) *Amoeba* as seen through a light microscope x 100. From:(http://faculty.clintoncc.suny.edu/facultymichael.gregory/files/Bio%20102%20lectures/protists/protists.htm). B) Electron Micrograph of a transverse section of a root tip of the bean *Phaseolus Vulgaris*. Source: de Duve (1984). C) A protein-protein interaction map 'interactome' Giot L, *et al*. Science (2003).

**Figure 32: Images of cells through the semiotic lens**
Source of images see Figure 31.

**Figure 33: The construction of indexicality.**
Electron micrograph and optical image of a cultured fibroblast
From Keith R Porter, Albert Claude, Ernest F Fullam, 'A study of tissue culture cells by electron microscopy: Methods and preliminary observations', *Journal of Experimental Medicine*, 1945, 81: 233-55, in p. 247.

**Figure 34: The distinctive nature of the Referent.**
Adapted from Pauwells 2006, Figure 1-1, pp. 4.

**Figure 35: The triangle of signification**

**Figure 36: The historical dimension of 'Objectivity'.**
Adapted from, Daston, et al. 2007, pp. 413.

## A.4. Interviews.

Semi structured interviews with three of the six authors of MBC were performed to gain insights in the process of its production. A set of questions, (8 to 12) were designed with the aim recollecting their experiences during the process of writing and image making. The following ones give an idea of the sort of questions asked to the interviewees.

1) Could you describe how MBC was born? How was the decision making process?

2) What made MBC distinctive from former textbooks in cell biology?

3) Could you tell me how the images were produced? What was your involvement with this?

4) Did the team ever disagree about a particular image or way of depicting a molecular process?

5) After so many editions of the book, what are your thoughts on the process of drawing invisible interactions that are in principle invisible?

6) The preface of the third edition, which appeared in 1994 states, I quote, 'with this edition we have ventured into full colour'. What did that venture signify? What did you di want to achieve by publishing in colour?

7) In reviewing the first edition of MBC JB Gourdon from the LMBC in Cambridge stated, I quote, 'It is a adventurous than many previous textbooks in cell biology in that it does not hesitate to make generalisations and to suggests possible mechanisms (where neither may be totally documented)' Do you have any comments on it?

Quotations from the interviews that are cited in the text are in between brackets and its location on the MP3 file indicated in the following format: (MRI 00.45.23) which means Martin Raff Interview 00 hours, 45 minutes and 23 seconds. JLI and KRI mean

Julian Lewis interview and Keith Roberts interviews respectively. The interviews are in the author's possession and could be requested for inspection at any time.

The grammar of the quotations follows directly their speech with no grammatical corrections made on them. The sign [?] inside the interviewee speech in writing means that it was inaudible or incomprehensible. The sign […] means an omission of the interviewee speech into the text because of it was too long and/or completely irrelevant for the point that was being made. Only dots, like, ….. , separating two pieces of speech from the interviewee express moments of silence and/or hesitation during the interviewee speech. Verbal expressions such as those of surprise, and laughs are not included in the text. The interview questions are protected by the UCL under the data protection registration project reference number: Z6364106/2007/1/23, section 19, medical research.

**A.5. Tables (quantitative data).** (See next page)

**Table 1 General Cytology De Robertis et al 1rst edition 1948**

| Chapter Number / Title / Categories | Ch 3<br>Morphological organisation of the cell | Ch 4<br>Submicroscope organisation of the cell | Ch 5<br>Morphology and functional significance of cytoplasm organelles | Ch 6<br>Plasma membrane and cell permeability | Ch 10<br>Enzymes and cell respiration | Ch 11<br>Visible manifestations of cellular activity | Ch 12<br>Differentiation, senescence and death of the cell | Total % of each category |
|---|---|---|---|---|---|---|---|---|
| **Optical Images** | 5 62.5 % | 0 0 % | 7 50 % | 0 0 % | 0 0 % | 8 47.05 % | 3 37.5 % | 28.15 % |
| **Electronic** | 0 0 % | 3 23.1 % | 3 21.4 % | 0 0 % | 0 0 % | 3 17.64 % | 5 62.5 % | 17.80 % |
| **Drawing of cells or cell components.** | 1 12.5 % | 2 15.38 % | 4 28.6 % | 1 20 % | 1 16.67 % | 2 11.76 % | 0 0 % | 15 % |
| **Models** | 0 | 1 | 0 | 2 | 0 | 0 | 0 | 0.43 % |
| **Cellular** | 0 0 % | 0 0 % | 0 0 % | 0 0 % | 0 0 % | 3 17.64 % | 0 0 % | 2.52 % |
| **e⁻ based** | 0 0 % | 1 7.69 % | 0 0 % | 2 40 % | 0 0 % | 0 0 % | 0 0 % | 6.81 % |
| **Molec. 3rd gen** | 0 0 % | 0 0 % | 0 0 % | 0 0 % | 0 0 % | 0 0 % | 0 0 % | 0 % |
| **Drawings. Apparatus Techniques. Gels. Diagrams. Molecules in their own. Hybrid images** | 2 25 % | 7 53.8 % | 0 0 % | 2 40 % | 5 83.33 % | 1 5.88 % | 0 0 % | 29.7 % |
| **Total number of images (figures) per chapter** | 8 | 13 | 14 | 5 | 6 | 17 | 8 | |

**Table 2 Cell Cytology De Robertis et al 3rd edition 1960**

| Chapter Number / Title / Categories | Ch 5<br>Submicroscopical organisation or ultrastructure of cells; methods of study | Ch 6<br>General organisation of the ground cytoplasm of the cell and the Golgi complex | Ch 7<br>Morphology and function of mitochondria | Ch 9<br>Plasma membrane and cell permeability | Ch 10<br>Morphological organisation of nucleus and chromosomes | Ch 16<br>Cytological and cytochemical aspects of cellular activity | Ch 17<br>Differentiation senescence of the cell | Total % of each category |
|---|---|---|---|---|---|---|---|---|
| **Optical Images** | 0 0 % | 3 16.67 % | 1 7.14 % | 4 30.77 % | 8 33.33 % | 5 21.74 % | 3 18.75 % | 18.34 % |
| **Electronic** | 5 35.7 % | 9 50 % | 7 50 % | 5 38.46 % | 7 29.2 % | 7 30.43 % | 8 50 % | 40.54 % |
| **Drawing of cells or cell components.** | 0 0 % | 1 5.55 % | 3 21.42 % | 0 0 % | 5 20.83 % | 1 4.35 % | 0 0 % | 7.45 % |
| **Models** | 3 | 3 | 3 | 3 | 2 | 5 | 4 | 3.28 % |
| **Cellular** | 0 0 % | 3 16.67 % | 1 7.14 % | 1 7.7 % | 1 4.16 % | 5 21.74 % | 2 12.5 % | 9.99 % |
| **e⁻ based** | 3 21.43 % | 0 0 % | 2 14.28 % | 2 15.38 % | 1 4.16 % | 0 0 % | 2 12.5 % | 9.67 % |
| **Molec. 3rd gen** | 0 0 % | 0 0 % | 0 0 % | 0 0 % | 0 0 % | 0 0 % | 0 0 % | 0 % |
| **Drawings. Apparatus Techniques. Gels. Diagrams. Molecules in their own. Hybrid images** | 6 42.86 % | 2 11.11 % | 0 0 % | 1 7.69 % | 2 8.33 % | 5 21.74 % | 1 6.25 % | 13.99 % |
| **Total number of images (figures) per chapter** | 14 | 18 | 14 | 13 | 24 | 23 | 16 | |

**Table 3 General Cytology De Robertis et al 4th edition 1965**

| Chapter Number / Title / Categories | Ch 6<br>Methods for cytological and cytochemical analysis | Ch 8<br>The plasma membrane | Ch 10<br>The cytoplasmic vacuolar system and microsomes | Ch 11<br>Mitochondria | Ch 19<br>Differentiation, growth renewal and senescence of cell populations | Ch 21<br>Mechanical activity and cell motion | Ch 22<br>Cellular basis of nerve conduction and synaptic transmition | Total % of each category |
|---|---|---|---|---|---|---|---|---|
| **Optical Images** | 6 31.58 % | 1 7.14 % | 3 15.78 % | 1 6.25 % | 1 33.33 % | 4 16 % | 1 5.26 % | 16.48 % |
| **Electronic** | 1 5.26 % | 10 71.43 % | 10 52.63 % | 6 37.5 % | 1 33.33 % | 10 40 % | 6 31.58 % | 38.82 % |
| **Drawing of cells or cell components.** | 1 5.26 % | 1 7.14 % | 0 0 % | 1 6.25 % | 0 0 % | 4 16 % | 2 10.53 % | 6.45 % |
| **Models** | 0 | 2 | 4 | 2 | 0 | 4 | 3 | 2.14 % |
| **Cellular** | 0 0 % | 1 7.14 % | 4 21.05 % | 1 6.25 % | 0 0 % | 1 4 % | 3 15.8 % | 7.75 % |
| **e- based** | 0 0 % | 1 7.14 % | 0 0 % | 1 6.25 % | 0 0 % | 3 12 % | 0 0 % | 3.63 % |
| **Molec. 3rd gen** | 0 0 % | 0 0 % | 0 0 % | 0 0 % | 0 0 % | 0 0 % | 0 0 % | 0 % |
| **Drawings. Apparatus Techniques. Gels. Diagrams. Molecules in their own. Hybrid images** | 11 57.9 % | 0 0 % | 2 10.53 % | 6 37.5 % | 1 33.33 % | 3 12 % | 7 36.84 % | 26.87 % |
| **Total number of images (figures) per chapter** | 19 | 14 | 19 | 16 | 3 | 25 | 19 | |

**Table 5 Cell and Molecular Biology. De Robertis et al 7th edition 1980**

| Chapter Number / Title / Categories | Ch 8<br>The cell membrane and permeability. intercellular interactions | Ch 9<br>The cytoskeleton | Ch 10<br>The endoplasmic reticulum and cell secretion | Ch 12<br>Mitochondria and oxidative phosphorylation | Ch 26<br>Cell differentiation | Ch 27<br>Cellular and molecular biology of the muscle | Ch 28<br>Cellular and molecular neurobiology | Total % of each category |
|---|---|---|---|---|---|---|---|---|
| **Optical Images** | 2 6.89 % | 4 23.53 % | 1 7.14 % | 1 4.76 % | 2 12.5 % | 1 8.33 % | 0 0 % | 9.02 % |
| **Electronic** | 8 27.59 % | 6 35.29 % | 4 28.57 % | 8 38.10 % | 1 6.25 % | 4 33.33 % | 6 20 % | 27.02 % |
| **Drawing of cells or cell components.** | 5 17.24 % | 2 11.76 % | 1 7.14 % | 3 14.28 % | 1 6.25 % | 0 0 % | 2 6.67 % | 9.04 % |
| **Models** | 8 | 4 | 6 | 2 | 1 | 5 | 11 | 5.28 % |
| **Cellular** | 4 13.8 % | 2 11.76 % | 1 7.14 % | 0 0 % | 1 6.25 % | 0 0 % | 6 20 % | 8.42 % |
| **e⁻ based** | 3 10.3 % | 2 11.76 % | 2 14.28 % | 1 4.76 % | 0 0 % | 5 41.67 % | 2 6.67 % | 12.78 % |
| **Molec. 3rd gen** | 1 3.45 % | 0 0 % | 3 21.43 % | 1 4.76 % | 0 0 % | 0 0 % | 3 10 % | 5.66 % |
| **Drawing. Apparatus Techniques. Gels. Diagrams. Molecules in their own. Hybrid images** | 6 20.7 % | 1 5.88 % | 2 14.28 % | 7 33.33 % | 11 68.75 % | 2 16.7 % | 11 36.67 % | 28.04 % |
| **Total number of images (figures) per chapter** | 29 | 17 | 14 | 21 | 16 | 12 | 30 | |

**Table 6** **Cell and Molecular Biology De Robertis et al** 8th edition **1987**

| Chapter Number / Title / Categories | Ch 4<br>Cellular membrane and permeability | Ch 5<br>Cellular interactions | Ch 6<br>The cytoskeleton and cell mobility | Ch 7<br>Cellular and molecular biology of the muscle | Ch 11<br>Mitochondria and oxidative phosphorylation | Ch 23<br>Cell differentiation | Ch 24<br>Cellular and molecular neurobiology | Total % of each category |
|---|---|---|---|---|---|---|---|---|
| **Optical Images** | 0 0 % | 2 13.33 % | 7 26.92 % | 1 7.7 % | 1 5 % | 6 18.18 % | 3 8.82 % | 11.42 % |
| **Electronic** | 2 11.11 % | 3 20 % | 8 30.77 % | 3 23.08 % | 4 20 % | 3 9.09 % | 5 14.71 % | 18.39 % |
| **Drawing of cells or cell components.** | 2 11.11 % | 3 20 % | 2 7.7 % | 1 7.7 % | 3 15 % | 7 21.21 % | 2 5.88 % | 12.66 % |
| **Models** | 6 | 5 | 3 | 7 | 3 | 3 | 13 | 5.71 % |
| **Cellular** | 2 11.11 % | 3 20 % | 2 7.7 % | 0 0 % | 0 0 % | 3 9.09 % | 7 20.59 % | 9.78 % |
| **e⁻ based** | 1 5.55 % | 1 6.67 % | 1 3.84 % | 6 46.15 % | 1 5 % | 0 0 % | 3 8.82 % | 10.86 % |
| **Molec. 3rd gen** | 3 16.7 % | 1 6.67 % | 0 0 % | 1 7.7 % | 2 10 % | 0 0 % | 3 8.82 % | 7.13 % |
| **Drawings. Apparatus Techniques. Gels. Diagrams. Molecules in their own. Hybrid images** | 8 44.4 % | 2 13.33 % | 6 23.1 % | 1 7.7 % | 9 45 % | 14 42.42 % | 11 32.35 % | 29.76 % |
| **Total number of images (figures) per chapter** | 18 | 15 | 26 | 13 | 20 | 33 | 34 | |

**Table 7 Molecular Biology of the Cell Alberts et al 1rst edition 1983**

| Chapter Number / Title / Categories | Ch 6 The plasma membrane | | Ch 7 Internal membranes and the synthesis of macromolecules | | Ch 9 Energy convertion, mitochondria and chloroplasts | | Ch 10 The cytoskeleton | | Ch 11 Cell growth and division | | Ch 12 Cell adhesion and the extracellular matrix | | Ch 13 Chemical signals between cells | | Total % of each category |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Optical Images** | 1 | 1.23 % | 1 | 1.43 % | 1 | 1.39 % | 8 | 9.19 % | 8 | 11.94 % | 4 | 5.63 % | 1 | 1.96 % | 4.68 % |
| **Electronic** | 13 | 16.05 % | 20 | 28.6 % | 9 | 12.5 % | 31 | 35.63 % | 12 | 17.91 % | 20 | 28.17 % | 1 | 1.96 % | 20.12 % |
| **Drawing of cells or cell components.** | 1 | 1.23 % | 5 | 7.14 % | 2 | 2.78 % | 3 | 3.45 % | 0 | 0 % | 8 | 11.27 % | 1 | 1.96 % | 3.97 % |
| **Models** | 16 | | 19 | | 11 | | 12 | | 6 | | 9 | | 29 | | 14.57 % |
| **Cellular** | 4 | 4.94 % | 9 | 12.8 % | 2 | 2.78 % | 3 | 3.45 % | 5 | 7.76 % | 6 | 8.45 % | 6 | 11.76 % | 7.42 % |
| **e- based** | 3 | 3.7 % | 4 | 5.71 % | 4 | 5.55 % | 9 | 10.34 % | 1 | 1.49 % | 2 | 2.82 % | 0 | 0 % | 4.23 % |
| **Molec. 3rd gen** | 9 | 11.11 % | 6 | 8.57 % | 5 | 6.94 % | 0 | 0 % | 0 | 0 % | 1 | 1.41 % | 23 | 45.1 % | 10.45 % |
| **Drawings. Apparatus. Techniques. Gels. Diagrams. Molecules in their own. Hybrid images** | 50 | 61.73 % | 25 | 35.71 % | 49 | 68.05 % | 33 | 37.93 % | 41 | 61.2 % | 30 | 42.25 % | 19 | 37.25 % | 49.16 % |
| **Total number of images (figures) per chapter** | 81 | | 70 | | 72 | | 87 | | 67 | | 71 | | 51 | | |

**Table 8 Molecular Biology of the Cell Alberts et al 2nd edition 1989**

| Chapter Number / Title / Categories | Ch 6 The plasma membrane | | Ch 7 Energy conversion, mitochondria and chloroplasts | | Ch 8 Intracellular sorting and the maintenance of cellular compartments | | Ch 11 The cytoskeleton | | Ch 12 Cell signalling | | Ch 13 Cell growth and division | | Ch 14 Cell adhesion, cell junctions and the extracellular matrix | | Total % of each category |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Optical Images** | 1 | 1.15 % | 1 | 1.33 % | 2 | 2.35 % | 12 | 13.33 % | 1 | 2.04 % | 7 | 9.33 % | 6 | 8.95 % | 5.5 % |
| **Electronic** | 14 | 16.09 % | 9 | 12 % | 15 | 17.65 % | 34 | 37.78 % | 1 | 2.04 % | 16 | 21.33 % | 17 | 25.37 % | 18.9 % |
| **Drawing of cells or cell components.** | 2 | 2.3 % | 3 | 4 % | 2 | 2.35 % | 1 | 1.11 % | 1 | 2.04 % | 1 | 1.33 % | 2 | 2.98 % | 2.3 % |
| **Models** | 22 | | 14 | | 31 | | 13 | | 27 | | 11 | | 9 | | 18.14 % |
| **Cellular** | 5 | 5.75 % | 2 | 2.67 % | 9 | 10.59 % | 3 | 3.33 % | 5 | 10.2 % | 6 | 8 % | 5 | 7.46 % | 6.86 % |
| **$e^-$ based** | 4 | 4.6 % | 5 | 6.67 % | 4 | 4.7 % | 8 | 8.89 % | 0 | 0 % | 2 | 2.67 % | 3 | 4.48 % | 4.57 % |
| **Molec. 3rd gen** | 13 | 14.94 % | 7 | 9.33 % | 18 | 21.2 % | 2 | 2.22 % | 22 | 44.9 % | 3 | 4 % | 1 | 1.49 % | 14.01 % |
| **Drawings. Apparatus Techniques. Gels. Diagrams. Molecules in their own. Hybrid images** | 48 | 55.2 % | 48 | 64 % | 35 | 41.2 % | 30 | 33.33 % | 19 | 38.8 % | 40 | 53.3 % | 33 | 49.25 % | 47.8 % |
| **Total number of images (figures) per chapter** | 87 | | 75 | | 85 | | 90 | | 49 | | 75 | | 67 | | |

**Table 9 Molecular Biology of the Cell Alberts et al 3rd edition 1994**

| Chapter Number / Title / Categories | Ch 10 + Ch 11<br>Membrane structure + Membrane transport | Ch 12<br>Intracellular compartments and protein sorting | Ch 13<br>Vesicular traffic in the secretory and endocytic pathways | Ch 14<br>Energy conservation, mitochondria and chloroplasts | Ch 15<br>Cell signalling | Ch 16<br>The cytoskeleton | Ch 19<br>Cell junction, cell adhesion and the extracellular matrix | Total % of each category |
|---|---|---|---|---|---|---|---|---|
| **Optical Images** | 2 2.5 % | 1 1.85 % | 0 0 % | 1 1.41 % | 1 1.45 % | 25 25.51 % | 3 4.35 % | 5.29 % |
| **Electronic** | 7 8.75 % | 9 16.67 % | 17 28.33 % | 7 9.86 % | 2 2.9 % | 34 34.7 % | 20 29 % | 18.6 % |
| **Drawing of cells or cell components.** | 1 1.25 % | 2 3.70 % | 3 5 % | 2 2.82 % | 2 2.9 % | 2 2.04 % | 3 4.35 % | 3.15 % |
| **Models** | 21 | 26 | 31 | 14 | 37 | 15 | 16 | 22.8 % |
| **Cellular** | 0 0 % | 2 3.70 % | 12 20 % | 1 1.41 % | 4 5.8 % | 3 3.06 % | 6 8.7 % | 6.09 % |
| **e⁻ based** | 4 5 % | 4 7.41 % | 4 6.67 % | 1 1.41 % | 0 0 % | 5 5.1 % | 5 7.25 % | 4.69 % |
| **Molec. 3rd gen** | 17 21.25 % | 20 37.04 % | 15 25 % | 12 16.9 % | 33 47.83 % | 7 7.14 % | 5 7.25 % | 23.20 % |
| **Drawings. Apparatus Techniques. Gels. Diagrams. Molecules in their own. Hybrid images** | 49 61.25 % | 16 29.63 % | 9 15 % | 47 66.2 % | 27 39.1 % | 22 22.45 % | 27 39.13 % | 38.96 % |
| **Total number of images (figures) per chapter** | 80 | 54 | 60 | 71 | 69 | 98 | 69 | |

**Table 10 Molecular Biology of the Cell Alberts et al 4th edition 2002**

| Chapter Number / Title / Categories | Ch 10 + Ch 11<br>Membrane structure + Membrane transport | Ch 12<br>Intracellular compartments and cell sorting | Ch 13<br>Intracellular vesicular traffic | Ch 14<br>Energy conversion, mitochondria and chloroplasts | Ch 15<br>Cell communication | Ch 16<br>The cytoskeleton | Ch 19<br>Cell junction, cell adhesion and the trancellular matrix | Total % of each category |
|---|---|---|---|---|---|---|---|---|
| **Optical Images** | 2 2.32 % | 3 5 % | 2 3.12 % | 3 4.22 % | 4 5.1 % | 33 33 % | 4 5.33 % | 8.3 % |
| **Electronic** | 4 4.65 % | 8 13.3 % | 16 25 % | 6 8.45 % | 1 1.26 % | 23 23 % | 21 28 % | 14.81 % |
| **Drawing of cells or cell components.** | 2 2.32 % | 2 3.33 % | 2 3.12 % | 0 0 % | 2 2.53 % | 1 1 % | 3 4 % | 2.33 % |
| **Models** | 26 | 34 | 29 | 20 | 46 | 20 | 13 | 26.86 % |
| **Cellular** | 4 4.65 % | 2 3.33 % | 10 15.6 % | 2 2.82 % | 4 5.1 % | 5 5 % | 4 5.33 % | 6 % |
| **e⁻ based** | 2 2.32 % | 2 3.33 % | 2 3.12 % | 2 2.82 % | 0 0 % | 5 5 % | 2 2.67 % | 2.75 % |
| **Molec. 3rd gen** | 20 23.25 % | 30 50 % | 17 26.6 % | 16 22.5 % | 42 53.2 % | 10 10 % | 7 9.33 % | 27.84 % |
| **Drawings. Apparatus Techniques. Gels. Diagrams. Molecules in their own. Hybrid images** | 52 60.46 % | 13 21.7 % | 15 23.44 % | 42 59.15 % | 26 33 % | 23 23 | 36 48 % | 38.4 % |
| **Total number of images (figures) per chapter** | 86 | 60 | 64 | 71 | 79 | 100 | 75 | |

**Table 11** **Molecular Biology of the Cell** **Alberts et al** **3rd edition 2008**

| Chapter Number / Title / Categories | Ch 10 + Ch 11<br>Membrane structure + Membrane transport | Ch 12<br>Intracellular compartments and cell sorting | Ch 13<br>Intracellular vesicular traffic | Ch 14<br>Energy conversion, mitochondria and chloroplasts | Ch 15<br>Mechanisms of cell communication | Ch 16<br>The cytoskeleton | Ch 19<br>Cell junction, cell adhesion and the extracellular matrix | Total % of each category |
|---|---|---|---|---|---|---|---|---|
| **Optical Images** | 3 3.6 % | 3 5.08 % | 2 2.70 % | 3 4.11 % | 4 4.55 % | 31 28.97 % | 7 8.54 % | 8.22 % |
| **Electronic** | 6 7.14 % | 8 13.56 % | 17 22.97 % | 6 8.22 % | 2 2.27 % | 23 21.49 % | 26 31.71 % | 15.34 % |
| **Drawing of cells or cell components.** | 0 0 % | 1 1.69 % | 3 4.05 % | 4 5.48 % | 2 2.27 % | 1 0.93 % | 1 1.22 % | 2.23 % |
| **Models** | 28 | 34 | 35 | 21 | 51 | 25 | 17 | 30.14 % |
| **Cellular** | 2 2.38 % | 3 5.08 % | 10 13.5 % | 1 1.37 % | 4 4.55 % | 7 6.54 % | 4 4.9 % | 5.47 % |
| **e- based** | 1 1.2 % | 1 1.69 % | 1 1.35 % | 1 1.37 % | 0 0 % | 6 5.6 % | 3 3.66 % | 2.12 % |
| **Molec. 3rd gen** | 25 29.76 % | 30 51 % | 24 32.4 % | 19 26 % | 47 53.4 % | 12 11.21 % | 10 12.2 % | 30.85 % |
| **Drawing. Apparatus Techniques. Gels. Diagrams. Molecules in their own. Hybrid images** | 47 56 % | 13 22 % | 17 23 % | 39 53.4 % | 29 33 % | 27 25.23 % | 31 37.80 % | 35.77 % |
| **Total number of images (figures) per chapter** | 84 | 59 | 74 | 73 | 88 | 107 | 82 | |